Archives of Dermatology and Syphilology

VOLUME 43 APRIL 1941 NUMBER 4

COPYRIGHT, 1941, BY THE AMERICAN MEDICAL ASSOCIATION

URTICARIA SOLARIS

REVIEW OF THE LITERATURE AND REPORT OF A CASE

HARRY L. ARNOLD JR., M.D.

HONOLULU, TERRITORY OF HAWAII

Urticarial wheals produced by exposure to sunlight have been reported rather infrequently in the literature, abundant though it is on subjects dealing with physical allergy and with photosensitization. Moreover, adequate attempts to define the responsible portion or portions of the spectrum have been made in only a few of the reported cases. These facts seem to justify a brief survey of available literature and the report of a case of urticaria caused by sunlight.

The comparative rarity of urticaria solaris is attested by the brevity with which it is treated in textbooks. In the 1910 edition of Stelwagon's textbook [1] there is no mention of it. Ormsby,[2] in 1937, remarked that it had been observed. Andrews,[3] in 1938, briefly referred to the case described by Duke [4] in 1923. Jadassohn,[5] in 1938, stated briefly that "urticaria solaris ('photogenica')" appears to be produced by radiation in the "longer wave, ultraviolet" region. Hopkins and Kesten,[6] in an extensive review of urticaria with particular reference to causation, did not mention sunlight as a cause; the total number of cases reviewed, however, was not given.

A few reported cases of urticaria produced by exposure to sunlight do not really belong in the category of urticaria solaris. Blum and

Read at the meeting of the Clinic, July 17, 1940.

1. Stelwagon, H.: Diseases of the Skin, Philadelphia, W. B. Saunders Company, 1910, p. 172.

2. Ormsby, O. S.: Diseases of the Skin, Philadelphia, Lea & Febiger, 1937, p. 146.

3. Andrews, G. C.: Diseases of the Skin, Philadelphia, W. B. Saunders Company, 1938, p. 164.

4. Duke, W. W.: Urticaria Caused by Light, J. A. M. A. **80**:1835 (June 23) 1923.

5. Jadassohn, J.: Dermatologie, Vienna, Weidmann & Co., 1938, p. 112.

6. Hopkins, J. G., and Kesten, B. M.: Urticaria: Etiologic Observations, Arch. Dermat. & Syph. **29**:358 (March) 1934.

Templeton [7] reported a case in which urticarial wheals could be reproduced by sunlight in all the sites of previous hypodermic injections of photodyn, a synthetic preparation of hematoporphyrin hydrochloride. Meyer-Betz [8] produced similar photosensitization in himself by a single intravenous injection of the same substance. Duke,[9] in 1926, reported a case in which the same seven urticarial wheals, grouped near one elbow, recurred with each fifteen second exposure of the area to sunlight; further exposure made them enlarge to the point of confluence. Dracoulides [10] reported a case in which emotion, fatigue, coitus or sunlight would produce urticaria. He did not state whether he thought coitus might act independently of the factors of emotion and fatigue. The condition in none of these 4 cases properly fits into the category of urticaria solaris, either because of a factitious element or regional "fixation" of the sensitization or because of the effectiveness of factors other than solar (or similar) radiation in eliciting the lesions.

A number of cases have been reported, presented before dermatologic societies or mentioned in discussion at meetings which may probably be properly classified as cases of urticaria solaris but which have been studied inadequately or not at all in regard to the wavelengths required for the formation of wheals. Oliver [11] presented a case of this kind before the Chicago Dermatological Society in 1925; there had not been time to study the case, and no further report seems to have been made. At the same meeting Foerster mentioned having studied 2 cases of urticaria due to sunlight for the presence of hematoporphyrinuria, without finding it; Goeckerman stated he had had a case in which improvement was caused by thyroid medication, and Sutton stated that he had observed several cases. Sellei [12] referred to the effectiveness of radiation from the cold quartz mercury vapor lamp and of sunlight filtered through glass in the production of wheals. Scheer [13] recently presented before the Section of Dermatology and Syphilis of the New York Academy of

7. Blum, H. F., and Templeton, H. J.: Sequel to Treatment with Photodyn, J. A. M. A. **108**:548 (Feb. 13) 1937.

8. Meyer-Betz, F.: Investigations on Biologic (Photodynamic) Activity of Hematoporphyrin, Deutsches Arch. f. klin. Med. **112**:476, 1913; cited by Blum and Templeton.[7]

9. Duke, W. W.: Physical Allergy as a Cause of Dermatoses, Arch. Dermat. & Syph. **13**:176 (Feb.) 1926.

10. Dracoulides, N. N.: Urticaria Due to Fatigue, Emotional Reactions, and Meteorologic Agents, Rev. franç. de dermat. et de vénéréol. **14**:174 (April) 1938; abstracted by Dr. H. H. Holman.

11. Oliver, E. A.: Urticaria Due to Sunlight, Arch. Dermat. & Syph. **12**: 408 (Sept.) 1925.

12. Sellei, J.: Urticaria Solaris, Arch. f. Dermat. u. Syph. **161**:32, 1930; abstracted by Dr. H. H. Holman.

13. Scheer, M.: Urticaria from Heat, Arch. Dermat. & Syph. **41**:1191 (June) 1940.

Medicine a patient sensitive to heat and to sunlight; he had been able to reproduce the lesions by exposure to a 100 watt tungsten-filament bulb held 6 inches (15 cm.) away for two minutes. An experiment of this kind, of course, combines both heat and light and is therefore inconclusive.

There are in addition to these 5 cases at least 12 in which some attempt has been made to define the active portion of the spectrum. Ward,[14] in 1905, and Ochs,[15] in 1910, are cited by Duke as having each reported a case of urticaria solaris in which "violet light" was found to be effective. Strictly speaking, this would mean a spectral band from approximately 4,000 to 4,500 angstrom units; actually it is extremely difficult to obtain such a band except with a spectrograph, for no single filter offers such convenient transmission characteristics.

Duke,[4] in 1923, reported the type case and proposed the name urticaria solaris. The patient was a woman, aged 43, who had suffered for four years from urticarial plaques throughout any cutaneous areas exposed to sunlight. Duke was able to reproduce the lesions by sunlight filtered through colorless or violet glass and also by electric light; roentgen rays were ineffective. Since ordinary glass absorbs light of wavelengths shorter than about 3,200 angstroms and since "violet glass" may be presumed to absorb most of the light between, roughly, 5,000 and 6,500 angstroms, one may conclude that the "suspect" spectral regions in this case are from 3,200 to 5,000 angstroms and the far red and infra-red. The patient was said to have had no hematoporphyrin in her blood or urine (it should be recalled that this report antedated most of the important work on porphyrin chemistry). Regional exhaustion of the reaction was attempted as a therapeutic measure, with only transitory relief.

Beinhauer,[16] in 1925, reported a case of urticaria solaris of three years' duration in a man of 20. The lesions could be reproduced by radiation from a cold quartz mercury vapor lamp, either direct or through the nickel oxide filter, as well as by sunlight; they were not produced by light from a carbon arc lamp or from any of several types of tungsten filament bulbs, by roentgen rays (¼ Holzknecht unit) or by either sunlight or radiation from a cold quartz mercury vapor lamp after filtration through glass, whether plain or colored. The first clear inference from these data is that all light transmitted through glass—all light

14. Ward, S. B.: Erythema and Urticaria with a Condition Resembling Angio-Neurotic Oedema Caused only by Exposure to the Sun's Rays, New York M. J. **81**:742, 1905; cited by Duke.[9]

15. Ochs, B. F.: Case of Urticaria Caused by the Sun's Rays, M. Rec. **78**: 193, 1910; cited by Duke.[9]

16. Beinhauer, L. G.: Urticaria Solaris, Arch. Dermat. & Syph. **12**:62 (July) 1925.

of wavelengths longer than approximately 3,200 angstroms, i. e., all the near ultraviolet rays, the entire visible spectrum and the infra-red rays—was unable to produce the lesions in this case. Moreover, since the earth's atmosphere cuts off the solar spectrum rather abruptly at about 3,000 angstroms, the effective spectral region for this patient would seem to lie between 3,000 and 3,200 angstroms. Still more accurate definition is possible, since the cold quartz mercury vapor lamp emits a line spectrum, not a continuum; the only wavelengths it supplies in this region of the spectrum are a rather bright pair of lines at approximately 3,126 and 3,132 angstroms and a much less intense pair at 3,022 and 3,033 angstroms. There are no other mercury lines within 500 angstroms of these in either direction except relatively faint ones at 2,967 and at 3,341 angstroms. So the wavelengths effective in activating the "triple response" in this patient seem to be accurately and fairly conclusively established, though Beinhauer himself was content to ascribe the reaction to the near ultraviolet portion of the spectrum, and, of course, other wavelengths (between 3,000 and 3,200 angstroms) might also be effective. The patient's failure to react to the incandescent sources is natural, since they were all lamps of relatively low efficiency, with a color temperature well below 3,000 Kelvin, and would have emitted only a very small amount of energy at wavelengths shorter than 3,200 angstroms.[17] The ineffectiveness of the carbon arc lamp is easily explained if uncored "hard" carbons were used, since the emission from an arc of this type has its energy largely confined to the three "CN bands," a molecular type of spectrum with three relatively broad bands of light between, roughly, 3,500 and 4,200 angstroms. The "crater" in the end of a soft core carbon, on the other hand, becomes incandescent and emits a continuous spectrum. The only further point of interest about this case is that a hypodermic injection of 6 drops of a solution of epinephrine before exposure to light markedly retarded and reduced the wheal formation, while injections of anterior and posterior pituitary did not affect it.

Frei,[18] in 1925, reported a case of sunlight urticaria in which, he stated, the short visible and long ultraviolet radiations were responsible. This terminology hardly permits evaluation in terms of angstroms, but such a range could scarcely exceed the broad limits of 3,000 and 5,000 angstroms.

Vallery-Radot, Blamoutier, Justin-Besançon and Saidman,[19] in 1926, reported another case, in a woman aged 44; they stated that mechanical

17. Film Characteristics: V, Photo Technique **2**:36 and 49 (April) 1940.

18. Frei, W.: Local Urticarial Skin Reactions to Sunlight, Arch. f. Dermat. u. Syph. **149**:124, 1925; abstracted by Dr. H. H. Holman.

19. Vallery-Radot, P.; Blamoutier, P.; Justin-Besançon, L., and Saidman, J.: Urticaria from the Sun's Rays, Bull. et mém. Soc. méd. d. hôp. de Paris **50**:1116 (June 25) 1926; abstracted, J. A. M. A. **87**:883 (Sept. 11) 1926.

irritation, roentgen rays and "electric light" would not reproduce the lesions. Since any type of "electric light" emits a continuous spectrum relatively rich in infra-red and visible wavelengths, with a rapid falling off of intensity (as compared with sunlight) toward the shorter wavelengths, this finding merely suggests that the effective spectral region is in the blue or ultraviolet, or roughly at 3,000 to 5,000 angstroms. This patient received autohemotherapy, without benefit.

Vallery-Radot, Blamoutier, Stéhelin and Saidman,[20] in 1928, reported another case of solar urticaria in which they found the effective wavelengths to extend throughout the visible spectrum, only ultraviolet and infra-red radiations being ineffective. This, again, might be expressed in angstroms as a range of approximately 4,000 to 7,000.

Wucherpfennig,[21] in 1928, reported 3 cases of this type of sensitization which were studied with several types of light source; the ultraviolet source used was the so-called Höhensonnenheit quartz mercury vapor lamp. He concluded that all 3 of his patients exhibited their greatest sensitivity to radiation in the near ultraviolet portion of the spectrum, presumably roughly at 3,000 to 4,000 angstroms, and that 2 of the 3 were reactive to rays only in this region, while the third reacted to visible light as well in all wavelengths except the red; this would represent a range of approximately 3,000 to 6,000 angstroms.

Weiss,[22] in 1932, reported a case in which radiation from the quartz mercury vapor arc lamp was effective in eliciting wheals. The range of such a source is considerable, but it is full of gaps, being a line spectrum. It has (in the range of sunlight) only the following (approximate) wavelengths in significant intensity: three in the near ultraviolet region (3,130, 3,340 and 3,650 angstroms), two in the violet (4,050 and 4,350 angstroms), one in the blue (4,950 angstroms), one in the green (5,450 angstroms) and one in the orange (5,950 angstroms).

Blum and West,[23] in 1937, reported a case in which they determined (using a 500 watt Mazda projection lamp and filters) that the spectral region effective in eliciting wheals was between 4,000 and 5,000 angstroms. They postulated that the sensitizing pigment was a carotenoid, since the absorption spectrum of carotenoids lies almost wholly within this blue and violet band.

---

20. Vallery-Radot, P.; Blamoutier, P.; Stéhelin, J., and Saidman, J.: Solar Urticaria, Bull. et mém. Soc. méd. d. hôp. de Paris **52**:1122 (July 5) 1928; abstracted by Dr. H. H. Holman.

21. Wucherpfennig, V.: Pathologic Hypersensitiveness to Light Rays: Three Cases, Arch. f. Dermat. u. Syph. **156**:520, 1928; abstracted by Dr. H. H. Holman.

22. Weiss, E.: Urticaria Solaris, J. Allergy **3**:192 (Jan.) 1932; abstracted by Dr. H. H. Holman.

23. Blum, H. F., and West, R. J.: Urticarial Response to Blue and Violet Light in Man, J. Clin. Investigation **16**:261 (March) 1937.

It is not possible, of course, to draw accurate conclusions from data arrived at by such a wide variety of methods, many of which are necessarily inexact. Some general observations of interest, however, can be made. There was just one rather narrow band in which some degree of sensitivity was exhibited in 9 of the 12 cases, between 4,000 and 5,000 angstroms. In the remaining 3 (that of Beinhauer and the first 2 of Wucherpfennig's) there was no sensitivity in this region, but sensitivity was found to the mercury line pairs at, roughly, 3,030 and 3,130 angstroms. The 12 cases can, then, be rather crudely divided into three groups: 5 in which there were reactions to violet light but not to ultraviolet rays in wavelengths shorter than 3,200 angstroms, 3 in which there were reactions to wavelengths shorter than 3,200 angstroms but not to violet or other visible light and 4 in which there were reactions to either or to both.

Blum and his associates [24] have clearly and repeatedly emphasized the importance of identifying, whenever possible, the wavelengths effective in eliciting such abnormal biologic responses. The line of reasoning is briefly this: Light, in order to activate any biologic or pathologic process, must be absorbed. The absorption of light by any substance always takes place—other things being equal—in a manner characteristic of that substance. Therefore, the wavelengths of incident light which are able to energize an abnormal process, such as wheal formation, are likely to coincide with the absorption spectrum of (the wavelengths characteristically absorbed by) the photosensitizing substance. This line of reasoning has already led to the identification in animals suffering from fagopyrism of a chlorophyll-derived porphyrin, phylloporphyrin, the absorption spectrum of which lies in the spectral range (chiefly 5,700-7,000 angstroms) characterized by yellow, orange and red, the same region of the spectrum in which these animals exhibit their photosensitivity.[25] Similarly, Blum and Schumacher [24a] were able to exculpate quinine (which their patient had been taking) as the photosensitizing agent in a case of unrecognized fulminating and fatal pellagra and beriberi with striking photogenic dermatitis. They showed that the patient was sensitive only to the same wavelengths (shorter than 3,130 angstroms) that elicit the delayed erythema response in normal persons,

24. (*a*) Blum, H. F., and Schumacher, I. C.: Abnormal Sensitivity to Light in a Case of Possible Landry's Paralysis, Ann. Int. Med. **11**:548 (Sept.) 1937. (*b*) Blum, H. F.: Photosensitization, ibid. **6**:877 (Jan.) 1933. (*c*) Blum, H. F.; Allington, H., and West, R. J.: An Urticarial Response to Light and Its Photophysiology, J. Clin. Investigation **14**:435 (July) 1935. (*d*) Blum and West.[23]

25. (*a*) Foerster, H. R., and Schwartz, L.: Industrial Dermatitis and Melanosis Due to Photosensitization, Arch. Dermat. & Syph. **39**:55 (Jan.) 1939. (*b*) Goldsmith, W. N.: Recent Advances in Dermatology, Philadelphia, P. Blakiston's Son & Co., 1936.

whereas the absorption spectrum of quinine barely overlaps the longer wave part of this region and the overlapping occurs in a region where epidermal transparency is relatively slight.[26] The same investigative technic has proved rather confusing in connection with hydroa aestivale, however; many investigators have felt [27] that the rather frequent association of porphyrinuria with this disease suggested an etiologic relation, but the absorption spectrums of the porphyrins (which all lie within the limits of 5,010 and 6,330 angstroms) [28] by no means coincide with the spectral region (3,000 to 5,000 angstroms) [25b] in which the sensitivity in cases of hydroa (when there is light sensitivity at all) is found. After a long career as suspected naturally occurring photosensitizing agents, the porphyrins are now coming to be regarded as merely inactive associates, or even products, of photosensitization reactions.[29]

The technic of defining the responsible regions of the solar spectrum in the production of any light dermatosis is not difficult if a few facts are borne in mind and a few preconceptions are not. The most reliable light source is the continuum (interrupted only by the narrow Fraunhofer absorption lines) emitted by the noonday sun. Atmospheric filtration cuts it off rather sharply in the ultraviolet region at approximately 3,000 angstroms. Another most useful source is the overloaded tungsten-filament incandescent lamp, such as the photoflood light or the more powerful projection lamps. Overloaded lamps are specified, because while all incandescent lamps deliver relatively less light in the blue and violet regions of the spectrum than is present in sunlight, this fault is indeed great in lamps not designed for operation under overloaded conditions. A simple practical experiment demonstrates this fact clearly: With color film balanced for use with photoflood lights, if a photograph is taken by sunlight and one by the light of an ordinary tungsten-filament lamp, the sunlight picture will be very blue and the other much too red.

The usual source of ultraviolet radiation is, of course, the air-cooled or water-cooled quartz mercury vapor arc lamp. As aforementioned, it delivers a wide but highly discontinuous spectrum; for example, there is only one moderately bright pair of lines between 4,400 and 5,400 ang-

26. Bachem, A., and Reed, C. I.: Skin and Radiation, Arch. Phys. Therapy **12**:581 (Oct.) 1931.

27. Senear, F. E., and Fink, H. W.: Hydroa Vacciniforme seu Aestivale, Arch. Dermat. & Syph. **7**:145 (Feb.) 1923. Goldsmith.[25b]

28. Turner, W. J., and Obermayer, M. E.: Studies on Porphyria: II, Arch. Dermat. & Syph. **37**:549 (April) 1938.

29. Brunsting, L. A.; Brugsch, J. T., and O'Leary, P. A.: Quantitative Investigation of Porphyrin Metabolism in Diseases of the Skin, Arch. Dermat. & Syph. **39**:294 (Feb.) 1939. Blum.[24b] Blum, Allington and West.[24c] Turner and Obermayer.[28]

stroms (fig. 1). The carbon arc source has also been discussed; it, too, may deliver a highly discontinuous spectrum under certain conditions, and the safest procedure, if it is to be used as a source of light, is to have a spectrogram made showing at least the qualitative spectral distribution of its emission.

The use of filters is full of pitfalls for the unwary. The assumption so often made that the color of a filter is a fairly good index of its optical properties is distinctly fallacious, for many filters have broad transmission bands well outside the spectral range that their color suggests. Yellow glass, for example, transmits at least green, orange and red, as well as infra-red rays, and many "violet" filters have a broad transmission band in the red, as well as in the blue and violet. The only safe method is to use Wratten or Corning filters and reference tables of their exact transmission characteristics. The one readily available "cut-

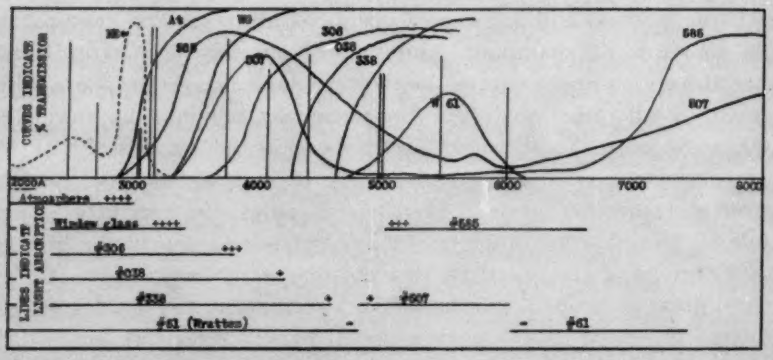


Fig. 1.—Spectrum analysis of filters used (modified after Bachem and Reed, from Blum and West). NE * signifies wavelengths producing the normal erythema response. Vertical lines indicate the mercury vapor lamp spectrum.

off" filter which can always be relied on is ordinary window glass, preferably, according to Blum and Schumacher,[24a] the kind that looks greenish when viewed edge-on. It absorbs almost all wavelengths shorter than about 3,200 angstroms and under some conditions may absorb even longer wavelengths, up to about 3,100 angstroms.

Other investigative approaches have been suggested. If the photosensitizing substance is present in the circulating blood, it might be possible to demonstrate abnormal absorption bands in the patient's blood serum. This is rendered somewhat difficult in the case of urticaria solaris, for the yellow color of normal serum makes for strong absorption of the very wavelengths—shorter than about 5,000 angstroms—which are most strongly suspected. If such absorption bands could be found, however, the problem would be enormously simplified, for at least one identifying property of the substance responsible for the dermatosis

would probably have been discovered. It might even be worth while to study the absorption spectrums of portions of the skin itself; the technical obstacles, though serious, are not insurmountable.

Another method of trying to identify the responsible wavelengths was used by Jensen and Hansen [30] in the investigation of a case of exogenous photosensitization of contact type. They projected a continuous spectrum of relatively high intensity directly on previously photosensitized portions of the patient's skin, achieving what might well be called a patch test with a rainbow. This method is remarkably free from most of the sources of error inherent in other procedures, with two exceptions. First, differences in relative intensity at different wavelengths (which are present in all light sources) are not easy to allow for properly. This might be overcome by the use of a vacuum thermopile, with which the absolute intensity of radiation in any selected portion of the spectrum could be readily determined. Only in such a way could comparable doses of light of different wavelengths be delivered. Second, it must be recalled that with this technic each single area of skin is receiving light of only one wavelength, not, as with filters, a "mixture" of wavelengths limited only by certain maxima or minima. Therefore if the sensitizing substance requires for its activation light from two or more different parts of the spectrum, it may not be energized by this procedure. For defining the region of the spectrum in which the absorption spectrum of the sensitizing substance lies, however, the method would seem to be nearly ideal; its only serious drawback is the considerable expense involved.

Callaway [31] has recently reported successful passive transfer by the Prausnitz-Küstner technic of a photosensitizing substance present in the blood serum of a patient with abnormal sensitivity to light. The principal value of this would seem to be in indicating some promise for efforts to find abnormal light absorption bands in the serum of such a person.

REPORT OF CASE

E. S., a 26 year old student of Caucasian (German, French and Irish) ancestry, came to the Clinic in April 1940, complaining that swelling and itching of his skin occurred whenever any portion of it was exposed to sunlight for more than about five minutes. He had first noticed this five years before while swimming; it happened on two occasions, and he thereafter took care to expose no more than his hands and face to the sun and for four years had no further trouble. He could recall no incident or change in his way of life or in his health which coincided with the onset of this sensitivity, except that he began smoking at about this time.

30. Jensen, T., and Hansen, K. G.: Active Spectral Range for Phytogenic Photodermatitis Produced by Pastinaca Sativa, Arch. Dermat. & Syph. **40**:566 (Oct.) 1939.

31. Callaway, J. L.: Passive Transfer of Light Sensitivity, Arch. Dermat. & Syph. **41**:889 (May) 1940.

In September 1939 he went on an archeologic expedition in the country outside of Honolulu, and after having been out only an hour or two noticed swelling and itching of the backs of both hands and the exposed portions of the wrists. His face was unaffected, a fact which, as he said, might well have been due to the customary stooping posture of an archeologist at work. The swelling subsided after about an hour but recurred on two or three similar occasions during the following few months.

In February 1940 his face swelled badly one morning during his ten minute walk to the University. He stated that this may not have indicated as sudden an increase in sensitivity as it seemed, since he often rode to school with friends and thus avoided exposure to the sun.

After that time his sensitivity remained approximately constant, with minor variations from day to day or during the day. From five to ten minutes of sunlight—direct, through light clouds or through window glass—on any part of his body produced a solid urticarial plaque throughout the exposed area (fig. 2). An intelligent and introspective person, he made a few gross observations of interest; his most sensitive area was the face, for even diffused light from the sky would produce erythema and moderate edema there within ten minutes; his

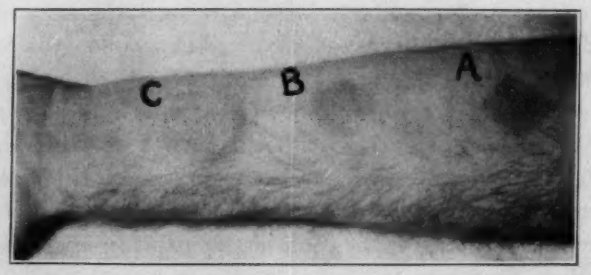


Fig. 2.—Cutaneous reactions after approximately (*A*) three minutes, (*B*) five minutes and (*C*) eight minutes of exposure to unfiltered noon sunlight through 1 inch (2.5 cm.) square holes in black paper.

elbow flexures and back were a close second, the back being so sensitive that a shirt would not protect it. He also observed on two occasions that the late afternoon sun, within an hour of setting, affected him little or not at all.

The family history was irrelevant. There were no siblings; his mother had died in her thirties of "pancreatitis" following a laparotomy, and his father was living and well, at about 60 years of age. Neither he nor his parents nor any other relative, so far as he knew, had ever had hay fever, urticaria, asthma, infantile "eczema" or migraine.

Examination disclosed a slender, pale young man of academic rather than athletic habitus, who appeared to be in good health. His hair and eyes were brown; his skin was free from lesions except for a few scattered pigmented cellular nevi, and his scalp and body hair were of normal masculine distribution and abundance. The mucous membranes looked normal; in particular, there was no suggestion of dietary deficiency in the appearance of the lips or tongue. His mentality was distinctly above average, and pupillary and tendon reflexes were active; no further neurologic examination was attempted. Auscultation, percussion and fluoroscopic examination of the chest revealed nothing abnormal. The blood

TABLE 1.—*Reactivity of Different Cutaneous Regions to Sunlight*

Region Tested	Type of Light	Time, Minutes	Reaction
Forearm, flexor (1 inch square areas)	Sunlight through light clouds	3	Erythema with punctate blanching
	Sunlight through light clouds	6	Same, plus appearance of cutis anserinus
	Sunlight through light clouds	9	Sharply defined wheal with narrow flare
Forearm, flexor (1 inch square areas)	Sunlight, direct noon	5	Erythema and cutis anserinus
	Sunlight, direct noon	8	Wheal and flare
Elbow flexure	Sunlight, direct noon	5	Wheal and flare
	Diffused daylight (shade)	10	No apparent reaction; slight itch
Face	Diffused daylight (shade)	10	Erythema, itching and slight edema

TABLE 2.—*Reactivity to Different Sources of Light*

Light Source (No Filters)	Distance, Inches	Time, Min.	Erythema Doses	Response
Sun	..	8	1	Erythema, wheal and flare; no subsequent erythema
Air-cooled quartz mercury vapor lamp	40	1	½	No reaction
		2	1	Delayed erythema only; no immediate reaction
		2½	1¼	Delayed erythema only; no immediate reaction
Photoflood lights (two; type R2)	20	20	...	Mottled erythema (heat response?) wheal and flare at this time in elbow flexure only
Carbon arc, soft core facing skin *	10	15	2	Delayed erythema only; no immediate reaction
Coolidge tube, 80 kv. peak, 5 ma., air cooled	12	1	1 (300 r)	No immediate reaction

* The instrument used was a standard Leitz carbon arc microscope lamp using one hard-cored and one soft-cored carbon, the incandescent crater of the latter being directed toward the patient. The condenser system was removed, so there was no filtration of the light.

TABLE 3.—*Reactivity to Different Parts of the Spectrum* *

Filter Used (Corning Glass Unless Stated Otherwise)	Transmission Characteristics, Angstroms	Erythema Time, Min.	Whealing Time, Min.	Wheal Quality
None	Above 3,000	5	8	Excellent
Colorless glass	Above 3,200	5	8	Excellent
No. 585 (blue purple ultra)	3,000 to 5,000 (plus infra-red)	6	12	Good
No. 306 (noviol O: straw)	Above 3,800	6	15	Fair
No. 038 (noviol A: straw yellow)	Above 4,200	9	No wheal after 30 minutes	
No. 507 (amethyst)	3,200 to 4,800 (plus infra-red)	12	No wheal after 30 minutes	
No. 338 (noviol C: yellow)	Above 4,600	16	No wheal after 30 minutes	
Wratten no. 61 (green)	4,900 to 6,100 (plus infra-red)	No erythema or wheal after 30 min.		

* Noon sunlight on the back was used in all tests.

pressure was nearly 130 systolic and 80 diastolic on several determinations. No abdominal viscera or masses could be felt.

Laboratory examinations showed mild anemia (11.5 Gm. of hemoglobin per hundred cubic centimeters of blood and 4,200,000 red cells per cubic millimeter) and moderate leukopenia (4,300 white cells per cubic millimeter, with 39 per cent polymorphonuclear leukocytes, 53 per cent lymphocytes, 7 per cent monocytes and 1 per cent eosinophils). The platelet count was 110,000 per cubic millimeter. The Wassermann, presumptive Kahn, diagnostic Kahn, Eagle and Laughlen reactions were all negative.

Extensive studies of the patient's photosensitivity were carried out; the results are tabulated in tables 1, 2 and 3, and the filter data are further analyzed in figure 1. The transmission characteristics of the Corning glass filters were taken from tables in the "Handbook of Chemistry and Physics;" [32] the form of the upper part of the chart is borrowed from Blum and West [23] and slightly modified according to Bachem and Reed.[26]

Passive transfer of the patient's photosensitivity was attempted by the injection of his freshly prepared blood serum intradermally into the skin of a normal person and subsequent irradiation of the site of injection with direct noon sunlight. There was a moderately strong immediate wheal reaction to the injections, but exposure of the sites to sunlight did not alter their appearance in the slightest degree. One site, kept covered as a control, looked just like the irradiated sites after they had been exposed to sunlight, and three control injections of serum from another normal person produced the same reaction as the injections of serum from the patient. The experiment was interpreted as having failed to demonstrate transferable photosensitizing substances in the patient's blood serum.

The absorption spectrum of the patient's serum was determined visually in a direct vision spectrometer by passing a beam of light from a photoflood light through a 100 mm. column of the serum. Strong absorption was observed throughout the violet and blue portions of the spectrum (ending at about 5,130 angstroms) and secondary bands of absorption, relatively narrow, between 5,320 and 5,480 and between 5,720 and 5,830 angstroms. Exactly the same pattern of light absorption was observed in a sample of serum from a normal person.

The patient was given a commercial preparation of histaminase (Torantil) in a dose of 5 tablets (25 "detoxifying units") three times a day. This was continued for two and a half weeks, without the slightest change in his sensitivity. No further treatment was attempted, because he had to leave Hawaii even before completion of all the investigative procedures that had been planned.

COMMENT

The fact that the patient reacted to sunlight at all establishes for him a high degree of sensitization to radiation in the near ultraviolet, visible or infra-red portions of the spectrum, i. e., any wavelengths longer than approximately 3,000 angstroms. The fact that he reacted as rapidly to sunlight transmitted through glass as to unfiltered sunlight means that in all probability he was not in the least sensitive to wavelengths between 3,000 and 3,200 angstroms. The fact that he was not sensitive to light

32. Handbook of Chemistry and Physics, ed. 22, Cleveland, Chemical Rubber Company, 1937.

from the air-cooled quartz mercury vapor lamp merely means that the absorption spectrum of the substance which rendered him photosensitive did not coincide with the emission spectrum of mercury at enough points to permit that type of light to energize it. It is likely, indeed, that the two spectrums did not coincide at all. The patient's low degree of sensitivity to the photoflood lights suggests that he was relatively insensitive to wavelengths longer than 6,000 angstroms,[17] particularly the infra-red; otherwise, it does not permit any helpful conclusions. His failure to react to roentgen rays is entirely natural, of course, since their wavelength is far removed from those found in sunlight. His failure to react to twice an erythema dose of radiation from the carbon arc lamp is extremely difficult to explain. Only two explanations seem possible: either the simultaneous exposure of this patient's skin to both "far" and "near" ultraviolet and visible radiations inactivates the photosensitization response, for some mysterious reason, or—and this seems far more plausible—light from this source exhibits a wider variation in intensity than a spectrogram made from it seems to indicate.

The filter data, while not conclusive by any means, are much more consistent and illuminating. Figure 1, showing the transmission curves, above, and blocking out of the absorption characteristics, below, indicates fairly clearly the portion of the spectrum to which the patient was most reactive. To radiation between 3,800 and 5,000 angstroms practically the same response (allowances being made for diminution in absolute intensity) was elicited as when the full spectrum was employed. When the band from 3,800 to 4,400 angstroms was cut out, the response was seriously depressed, and an even more decided effect was observed when this band was passed and the narrow strip from 4,800 to 5,000 angstroms was removed. The absence of any response to thirty minutes of sunlight through the Wratten green gelatin filter no. 61 completely exonerates not only the green but, more important, the entire infra-red portion, which this filter freely transmits. In summary, then, the portion of the spectrum in which this patient's sensitivity lies appears to extend from 3,800 to about 5,000 angstroms, and it does not coincide with the four fairly intense mercury lines in and adjacent to that region.

SUMMARY

Urticaria solaris is a photogenic dermatosis characterized by the formation of a wheal throughout any area of skin immediately on exposure of that area to light of sufficient intensity and proper wavelength. The active spectral region appears to differ in different cases but has usually been found to be in the violet and blue portions of the spectrum and occasionally in the near ultraviolet. It seems probable that the most rational therapeutic approach consists in an attempt to identify the exact wave-

lengths required to energize the reaction and thereby to identify, through its absorption spectrum, the photosensitizing substance. Methods of attacking this problem have been discussed and described, and their application in 1 case has been described and evaluated. The oral administration of histaminase failed to alter the sensitiveness to light in the case of urticaria solaris herein reported.

Mr. Paul Gow, spectroscopist at the Hawaiian Sugar Planters' Association Experiment Station, assisted in working out the problems of optical physics involved. Dr. H. H. Holman, Detroit, abstracted several articles not available either in the original or in abstract in Hawaii.

CLINICAL RESPONSE OF CERTAIN DERMATOLOGIC DISEASES TO SULFATHIAZOLE

LAWRENCE G. BEINHAUER, M.D.

ALFRED F. KNOLL, M.D.
AND
SAMUEL R. PERRIN, M.D.
PITTSBURGH

The response of certain dermatologic diseases to sulfanilamide is well established, and the literature on the subject has been adequately reviewed. Because sulfathiazole [1] appeared to be more effective than sulfanilamide for streptococcic infections,[2] on a par with sulfapyridine for pneumococcic infections [3] and superior to both for staphylococcic infections,[4] the clinical trial of sulfathiazole in the treatment of certain dermatologic diseases seemed to be indicated, particularly for those in which staphylococci or streptococci are etiologically concerned.

This paper submits data on the clinical effectiveness and the toxic side effects of sulfathiazole which justify a trend toward the use of this drug. The decision as to the choice of drug must, of course, be based on the proper evaluation of sufficient accumulated data.

CLINICAL OBSERVATIONS WITH SULFATHIAZOLE

A total of 103 patients were treated with sulfathiazole, 58 of whom had failed to respond to other forms of treatment. The majority of these patients (89) were treated with sulfathiazole alone, and the

From the Department of Dermatology and Institute of Pathology, the Western Pennsylvania Hospital.

1. The Maltbie Chemical Company, of Newark, N. J., and E. R. Squibb & Sons, New York, supplied the sulfathiazole used in this study.

2. Cooper, F. B.; Gross, P., and Lewis, M.: The Chemotherapeutic Evaluation of Sulfanilamide Derivatives of Heterocyclic Amines, Proc. Soc. Exper. Biol. & Med. **42**:421, 1939.

3. McKee, C. M.; Rake, G.; Greep, R. O., and van Dyke, H. B.: The Therapeutic Effect of Sulfathiazole and Sulfapyridine, Proc. Soc. Exper. Biol. & Med. **42**:417, 1939. Barlow, O. W., and Homburger, E.: Specific Chemotherapy of Experimental Staphylococcus Infections with Thiazole Derivatives of Sulfanilamide, ibid. **42**:792, 1940.

4. Barlow, O. W., and Homburger, E.: Thiazole Derivatives of Sulfanilamide and Experimental Beta Hemolytic Streptococcal and Pneumococcal Infections in Mice, Proc. Soc. Exper. Biol. & Med. **43**:317, 1940. Carroll, G.; Kappel, L., and Lewis, B.: Sulfathiazole: Clinical Investigations, J. A. M. A. **115**:1350 (Oct. 19) 1940.

remainder (14) were allowed to continue the ineffective local applications used prior to the sulfathiazole therapy. The dosage was uniform, consisting of 0.5 Gm. tablets four times daily, but was modified for children according to age.

Infectious Eczematoid Dermatitis.—The patients with this disease, the duration being seven days to five years, were treated for seven to forty-eight days, with an average treatment time of fourteen days. Thirteen were clinically cured; 5 manifested pronounced clinical improvement, and 1 was not improved. Recurrences were noted in 3 cases after withdrawal of the drug but promptly disappeared on readministration. Toxic reactions were encountered in a patient suffering from acute toxemia of pregnancy, in whom nausea and vomiting developed after seven days of medication. On readministration of the drug no toxic symptoms were noted. A patient with acute pulmonary tuberculosis after twenty-three days of medication had a sharp rise in temperature (103 F.), chills, nausea, weakness and muscular pains, all of which disappeared promptly with the cessation of medication. Because of the pronounced clinical response of the cutaneous manifestations, readministration of sulfathiazole was unnecessary. A third patient had nausea, vomiting and diarrhea but tolerated the drug on readministration. In another patient, suffering from acute exfoliative dermatitis following arsphenamine therapy, nausea and vomiting developed from the administration of sulfapyridine but sulfathiazole was tolerated without ill effects. Cultures were obtained in 9 cases and yielded hemolytic Staphylococcus aureus 7 times and Streptococcus haemolyticus associated with Staphylococcus pyogenes in 2.

Acne Vulgaris.—This study was limited to the pustular type of acne vulgaris. The duration of the disease varied from one to eight years. Seven of the patients in this group had resisted all previous forms of therapy, including ten to sixteen roentgen ray treatments. To these sulfathiazole alone was given. Two of this group were clinically cured and remained so during a six month period of observation; 3 were decidedly improved, and 2 were not improved. The remaining 5 patients, previously untreated, were given a three week preliminary course of sulfathiazole therapy alone, consisting of 2 Gm. of the drug daily prior to the contemplated roentgen ray therapy. A pronounced involution of the pustular lesions was noted within seven to fourteen days, and a complete resolution of the acne was then obtained after eight weekly roentgen ray treatments (75 r unfiltered roentgen rays). These patients have remained free from the disease to date, three months after cessation of treatment. Cultures were obtained in 8 of these cases and yielded hemolytic Staph. aureus six times and Staphylococcus albus twice. Although this study of the treatment of acne vulgaris with sulfathiazole is far too limited and the period of observation too short to evaluate

the final clinical result or to draw conclusions from this method of therapeutic procedure, it seems to support further investigation of this persistent and rebellious type of acne. In no case did we note any hypersensitivity to roentgen rays from administration of sulfathiazole.

Furunculosis.—Of 15 patients with furunculosis 3 were clinically cured in three days, 3 in five days, 2 in seven days and 1 each in eight, ten and fourteen days, and 4 were unaffected by this therapy. Ten had the local form of the disease and 5 the generalized form, in 1 complicating acute exfoliative arsenical dermatitis. The youngest of this group was 8 months of age and the oldest 70 years. Two reactions were noted: In 1 patient, a man aged 34, blurred vision, nausea, profound muscular weakness and mental symptoms developed, and in another a rapid rise in temperature developed twenty-four hours after the administration of sulfathiazole and reached a peak of 106 F. two days later. The temperature promptly receded after withdrawal of administration of the drug and returned to normal after the last furuncle had undergone involution. Readministration of the drug did not cause recurrence of the febrile reaction. Incidentally, the acute exfoliative arsenical dermatitis with which the latter patient was also suffering manifested decided improvement after the involution of the furunculosis. Cultures were obtained in 9 cases and yielded hemolytic Staph. aureus six times, Staph. pyogenes twice and Str. haemolyticus once.

Impetigo Contagiosa.—Six of the patients with this disease had proved resistant and refractory to the usual therapeutic measures, but 2 were clinically cured in three days and 1 each in two, four, five and seven days with sulfathiazole alone. Of the 7 patients who had received no previous treatment 3 were clinically cured in three days and 4 in four days with this drug alone. No toxic manifestations were noted, and 5 of this group were between the ages of 3 to 10 years. Cultures obtained in 7 cases revealed a mixture of hemolytic Staph. aureus and Str. haemolyticus five times and Str. haemolyticus alone twice.

Lupus Erythematosus.—Of 12 patients with discoid lupus erythematosus of one to twenty-five years' duration, 1 was clinically cured in twenty-one days, 2 showed pronounced improvement and 9 were unimproved. Two of the most serious reactions were encountered in this group. Two patients presented similar reactions on the tenth and twelfth day of treatment respectively. This reaction consisted of a sharp rise in temperature (103 to 105 F.), pronounced cyanosis with no associated dyscrasia, nausea, vomiting, intense and persistent muscular weakness lasting ten to fourteen days, blurred vision, albuminuria and mental symptoms. No cutaneous manifestations such as those recorded by Barber [5] were observed, but readministration of the drug caused recur-

5. Barber, H. W.: Lupus Erythematosus: The Effects of Sulfonamides, Lancet **1**:583, 1940.

rence of toxic symptoms. This condition we believe was a true idiosyncrasy to the drug. Focal reaction was noted in all local lesions, accompanied by tenderness, tingling and pruritus. Five other patients in this group complained of burning, tingling and tenderness in the local lesions, and pronounced sensitivity to sunlight was observed. Cultures were obtained from infected teeth in 1 patient and from the antrum of the other patient who had the severe reaction. Streptococcus viridans and hemolytic Staph. aureus were found in each instance.

Sycosis Barbae.—Four of the 9 patients were clinically cured, 2 manifested pronounced improvement and 3 were unaffected by treatment. Improvement was noted as early as seven days, and the clinical cures were obtained in fourteen, twenty-one, twenty-one and twenty-four days respectively. Recurrences occurred in 2 instances as a result of withdrawal of the drug because of toxic manifestations but promptly cleared on readministration. One patient received this drug for one hundred and ten days without ill effects. Toxic manifestations were noted in 2 patients and consisted of nausea, vomiting, dizziness, headache and profound muscular weakness. Cultures from the local lesions were obtained in 7 of the 8 cases and yielded hemolytic Staph. aureus four times, Str. haemolyticus once and Staph. albus twice.

Other Conditions.—Secondary pyogenic infection and lymphangitis complicating dermatophytosis responded quickly. Seven patients were treated; 6 were clinically cured, and 1 showed pronounced improvement within three to seven days. The accompanying dermatophytosis was unaffected. Three of these patients were permitted to continue with boric acid dressing used prior to the sulfathiazole therapy, but the remaining 4 were treated with sulfathiazole alone. Cultures were obtained in all cases and yielded hemolytic Staph. aureus four times, Bacillus pyocyaneus once and Str. haemolyticus twice. Two patients with recurrent erythema multiforme of five and twelve months' duration were clinically cured in eight and thirty-two days respectively with sulfathiazole and remained well during a six month observation period; a third was not benefited. Cultures from 2 patients yielded hemolytic Staph. aureus. A clinical cure of recurrent erythema nodosum of two years' duration was obtained in fourteen days with sulfathiazole. Of the 2 cases of folliculitis decalvans, in 1 there was pronounced improvement while in the other the therapy was ineffective. The cultures in both cases yielded a mixture of hemolytic Staph. aureus and Str. haemolyticus.

Failures with sulfathiazole therapy were encountered in 1 case of pemphigus erythematodes (Senear-Usher), 2 cases of dermatitis herpetiformis, 2 cases of herpes zoster and 2 cases of acute generalized lichen planus.

COMMENT

This series consisted of 103 patients with sixteen dermatologic diseases. The majority of the patients were male adults. The group age range was 3 months to 70 years. From an analysis of the available literature it may be stated that treatment with sulfanilamide and its derivatives has produced curative and beneficial results. It appears that furunculosis, erythema multiforme, impetigo contagiosa, acute disseminated lupus erythematosus and streptococcic lymphangitis have been most benefited by its use. Of this group, acute disseminated lupus erythematosus has been most widely studied. Although reported in smaller numbers, chronic lupus erythematosus, sycosis vulgaris, erythema nodosum and other dermatologic conditions have responded favorably to this type of therapy in sufficient instances to warrant continued clinical investigation. Our experience with sulfathiazole closely parallels the experience of those who have used other sulfanilamide compounds. We found sulfathiazole to be an efficacious mode of therapy in the treatment of acute infectious eczematoid dermatitis, furunculosis, impetigo contagiosa, pyogenic lymphangitis, blepharitis marginalis and erythema multiforme and to be beneficial in sycosis vulgaris. Special attention is called to the response of the pustular type of acne vulgaris. Our results have been gratifying and warrant further study in a larger series of cases. The response of discoid lupus erythematous was encouraging but not so pronounced or spectacular as the experience of those who had used sulfanilamide therapy in the treatment of the acute disseminated type. Failures with sulfathiazole therapy were experienced in the treatment of pemphigus, pemphigus erythematodes (Senear-Usher), dermatitis herpetiformis, herpes zoster and lichen planus. With these, excepting pemphigus, the clinical administration of sulfathiazole may not have been so definitely indicated, for instance, as for impetigo contagiosa or streptococcic lymphangitis, in which the pyogenic role is recognized.

On the basis of clinical studies of other types of diseases treated with the sulfanilamide compounds,[6] sulfathiazole appears to be less toxic than sulfanilamide, decidedly less than sulfapyridine and probably better suited for the ambulatory patient than either of the other two. It is just as good in controlling streptococcic infections and definitely superior in those caused by the staphylococcus. The culture findings in our series appear to bear out these contentions, and the best results were obtained by us in the group of diseases in which pyogenic infection played an etiologic role.

---

6. Flippin, H. F.; Schwartz, L., and Rose, S. B.: The Comparative Effectiveness and Toxicity of Sulfathiazole and Sulfapyridine in Pneumococcic Pneumonia, Ann. Int. Med. **13**:2038, 1940. Knoll, A. F.: Sulfathiazole in the Treatment of Pneumonia, M. Rec. **152**:335, 1940.

Sulfathiazole produces toxic manifestations, but in our experience these were of the minor type. Blood dyscrasia or urolithiasis medicamentosa [7] was not encountered, but albuminuria was present on occasion. Nausea, vomiting, diarrhea, cyanosis, febrile reaction, dizziness, blurred vision, headache, mental symptoms and profound muscular weakness were the most common toxic symptoms. Fortunately, these subsided with the withdrawal of the drug and did not recur on readministration except in 2 instances. No evidence of cutaneous manifestations was observed. The lack of major toxic symptoms, such as have been reported with the other sulfanilamide compounds, is probably due to the lesser toxicity of sulfathiazole, although the smaller doses given in our series

Dermatologic Diseases Treated with Sulfathiazole

Diseases	Number of Cases	Clinical Cures	Pronounced Improvement	No Improvement
Infectious eczematoid dermatitis	19	13	5	1
Acne vulgaris	12			
Sulfathiazole treatment following unsuccessful roentgen ray therapy	7	2	3	2
Sulfathiazole treatment preceding roentgen ray therapy	5	5	..	..
Furunculosis	15	11	..	4
Impetigo contagiosa	13	13	..	..
Lupus erythematosus	12	1	2	9
Sycosis vulgaris	9	4	2	3
Lymphangitis complicating dermatophytosis	7	6	1	..
Blepharitis marginalis	2	2	..	..
Dermatitis herpetiformis	2	..	..	2
Erythema multiforme	3	2	..	1
Herpes zoster	2	..	..	2
Acute generalized lichen planus	2	..	..	2
Folliculitis decalvans	3	..	1	1
Erythema nodosum	1	1	..	..
Pemphigus erythematodes (Senear-Usher)	1	..	..	1
Pemphigus	1	..	..	1
Totals	103	60	14	29

and the type of disease treated may also have been factors. The toxic manifestations which were encountered, although of minor degree, are significant enough to forewarn against the potential dangers of sulfathiazole, even though clinical experience has taught that it is less toxic than the other sulfonamide compounds.

It is not the purpose of this paper to offer sulfathiazole as a panacea in the treatment of pyogenic dermatoses or to ask that recognized dermatologic therapy for such relatively benign conditions as impetigo contagiosa, furunculosis and erythema multiforme be discarded in its favor. We wish merely to call attention to its therapeutic efficiency in these diseases and offer it as another therapeutic approach when

7. Knoll, A. F., and Cooper, F. B.: Clinical Urolithiasis Medicamentosa Due to Sulfathiazole, Urol. & Cutan. Rev. **44**:292, 1940. Gross, P.; Cooper, F. B., and Scott, R. E.: Urolithiasis Medicamentosa, ibid. **44**:205, 1940.

recognized therapy fails or perhaps as a substitution therapy in selected cases. It offers a promising, effective and practical form of therapy well suited to the ambulatory patient. It is our hope that this paper will stimulate further clinical investigation.

SUMMARY

One hundred and three patients with sixteen representative dermatologic diseases have been treated with sulfathiazole and the results tabulated.

The effectiveness of sulfathiazole has already been shown clinically and experimentally to be equal to or greater than that of sulfanilamide or sulfapyridine for infections ordinarily treated by sulfonamides.

Like other sulfanilamide compounds, sulfathiazole produces toxic manifestations. These, however, have been less severe and less numerous than those encountered with sulfanilamide and sulfapyridine therapy.

The results of sulfathiazole therapy in the treatment of certain dermatologic diseases are promising and indicate the probable trend which might be expected from this form of therapy.

LICHEN PLANUS ET ACUMINATUS ATROPHICANS (FELDMAN)

FOLLICULITIS DECALVANS ET LICHEN SPINULOSUS (LITTLE)

FRANCIS A. ELLIS, M.D.
BALTIMORE
AND
HAYDEN KIRBY-SMITH, M.D.
WASHINGTON, D. C.

In 1922 [1] and 1936 [2] Feldman presented detailed discussions of the subject of folliculitis decalvans et lichen spinulosus of Graham Little. According to Feldman, numerous investigators have studied this interesting disease and have reported it or closely similar conditions under the following titles: folliculitis decalvans et atrophicans (Little),[3] *folliculite destructive des régions velues* (Quinquand), folliculitis decalvans et lichen spinulosus (Ormsby,[4] Senear,[5] Graham Little [6] and others), lichen spinulosus et folliculitis atrophica sycosiformis capillitii (Zurhelle and Beijerinch), lichen albus (von Zumbusch), dermatitis lichenoides chronica atrophicans (Csillag), lichen planus sclerosus et atrophicus (Hallopeau), *lichen plan atrophique* (Hallopeau), *lichen plan sclereaux keloidiformis* (Pawlow), lichen planus morphoeicus (Crocker), lichen planus seu spinulosus (Crocker, and Adamson [7]), folliculitis decalvans et atrophicans (McCarthy [8]), keratosis follicularis

1. Feldman, S.: Lichen Planus et Acuminatus Atrophicans; Lichen Plan Atrophicus, Lichen Plan Sclereux, Hallopeau; Lichen Ruber Planus Keloidiformis, Pawlow; Lichen Planus Morphoeicus, Crocker; Lichen Albus, von Zumbush, Arch. Dermat. & Syph. **5**:102 (Jan.) 1922.

2. Feldman, S.: Lichen Planus et Acuminatus Atrophicans, Folliculitis Decalvans et Lichen Spinulosus of Little, Arch. Dermat. & Syph. **34**:378 (Sept.) 1936.

3. Little, E. G.: Folliculitis Decalvans et Atrophicans: Case Report, Brit. J. Dermat. **37**:183, 1915.

4. Ormsby, O. S.: Folliculitis Decalvans and Lichen Spinulosus, Arch. Dermat. & Syph. **1**:471 (April) 1920.

5. Senear, F. E.: Folliculitis Decalvans and Lichen Spinulosus: A Clinical Combination, Arch. Dermat. & Syph. **2**:198 (Aug.) 1920.

6. Little, E. G.: Lichen Spinulosus et Folliculitis Decalvans, Proc. Roy. Soc. Med. **14**:67, 1921.

7. Adamson, H. G.: Lichen Planus Seu Spinulosus, Brit. J. Dermat. **17**:39, 1905.

8. McCarthy, L.: Diagnosis and Treatment of Diseases of the Hair, St. Louis, C. V. Mosby Company, 1940.

decalvans (McCafferty [9]) and lichen planopilaris of Pringle (Fruchtbaum [10]).

A review of the literature and the presentation of our cases support Feldman's contention that Graham Little's folliculitis decalvans et lichen spinulosus is the same as lichen planus et acuminatus atrophicans. Feldman emphasized the fact that the pustules in folliculitis decalvans were not present in the patients he observed. He stated that Graham Little [11] had recognized an association or relation between cicatricial alopecia and acuminate lichen planopilaris of the scalp and of other hairy regions, such as the external genitalia in women. In 1936 Hunt [12] reported 73 cases of lichen planus of the vulva. In 48 per cent of them some form of atrophic lichen planus was found elsewhere; in 20 per cent the lesion was restricted to the vulva. The author considered lichen planus to be an etiologic factor in leukoplakia of the vulva and concluded that the atrophic stage of lichen planus was a form of kraurosis vulvae. One patient in Hunt's series in addition to having lichen planus of the vulva, which subsequently showed features of kraurosis, presented atrophic lichen planus of the scalp. Acuminate papular lesions were present at the hairy margin of the areas of alopecia.

Since Feldman's last article there have appeared several reports containing facts illustrating certain concepts of lichen planus et acuminatus atrophicans. In Traub's [13] patient the lesion was on the scalp and trunk and in the mouth. The histologic observations were typical except for lack of discernible atrophy. An unusual feature in Corsi's [14] case was the loss of the nails (onychomadesis), which was apparently due to atrophy of the nail beds. Rostenberg's [15] patient had had lesions for thirty years with atrophic areas in the scalp. In discussing Rostenberg's report, Feldman said that the condition was not a classic example

9. McCafferty, L. M.: Folliculitis Decalvans et Atrophicans (Little), Arch. Dermat. & Syph. **18**:514 (Oct.) 1928.

10. Fruchtbaum, L. M.: Lichen Planopilaris (Pringle): Case Report, Arch. Dermat. & Syph. **42**:156 (July) 1940.

11. Little, E. G.: An Undescribed Variety of Lichen Planus, Dermat. Wchnschr. **91**:1203, 1930.

12. Hunt, E.: Leucoplakia Vulvae, Kraurosis Vulvae, and Lichen Planus of the Vulva, Brit. J. Dermat. **48**:53, 1936.

13. Traub, E. F.: Lichen Planus et Acuminatus Atrophicans (Folliculitis Decalvans et Lichen Spinulosus of Little), Arch. Dermat. & Syph. **36**:888 (Oct.) 1937.

14. Corsi, H.: Lichen Planus Associated with Atrophy of Nail Matrix and Hair Follicles on Scalp, Proc. Roy. Soc. Med. **30**:198, 1937.

15. Rostenberg, A.: Folliculitis Decalvans et Atrophicans (Little) or Lichen Planus Acuminatus et Atrophicans (Feldman), Arch. Dermat. & Syph. **38**:668 (Oct.) 1938.

of lichen planus et acuminatus atrophicans. Kren [16] compared the clinical atrophic picture of lichen planus et acuminatus atrophicans to that of lupus erythematosus favus and pseudopelade. Jonquières [17] had a patient with atrophic lesions on the scalp and typical lichen planus papules in the mouth, on the glans penis and on the upper extremities. Bacciero [18] compared the alopecia to the pseudoareata of Brocq.

REPORT OF CASES

Case 1.—E. C., a white woman aged 22, was first seen on May 29, 1939, with a generalized eruption of one year's duration. There were no lesions on the face, on the dorsa of the fingers or on the mucous membranes. On the extremities the eruption consisted principally of groups, 1 cm. in diameter or slightly larger, of angulated, shiny, flat-topped papules in moderately well defined areas of pigmentation. There was evidence of slight atrophy in some of the areas. On the body there were many discrete, slightly inflamed, follicular keratotic papules, 2 mm. in diameter or slightly smaller. Some were arranged in corymbose groups. When this lesion underwent involution there remained a light brown pigmentation.

The patient's past history and the results of physical examination and laboratory tests were essentially negative as far as the cutaneous condition was concerned.

A biopsy specimen was taken from an area containing the small keratotic plugs. Under low power magnification the epidermis appeared to be normal, although perhaps the number of layers of rete cells was slightly diminished. There was some irregular acanthosis. The horny layer was slightly increased without parakeratosis. In some parts of the corium there was a sparse perivascular and perifollicular infiltrate. A striking feature was the follicular plugging. Many of the follicles were dilated and contained large cones of keratin; the walls were atrophic and consisted of few layers of flattened retelike cells. Surrounding the base of the follicles there was a dense mononuclear cell infiltrate which encroached on the epidermis. It resembled the band of cells usually seen in the subpapillary layer of a typical section of lichen planus. The elastic tissue appeared to be slightly fragmented.

Case 2.—Mrs. G. E. W., white, aged 60, was seen in February 1937 with generalized typical lichen planus. The lesions were more extensive in the submammary region, on the lower part of the back and on the arms and forearms. There were a few white punctate areas of leukoplakia on the mucous membranes of both cheeks. After a few weeks' treatment with fractional doses of roentgen rays and injections of mercury bichloride, the character of the eruption changed. Much of the eruption had disappeared or was undergoing involution. On the flexural surfaces of the wrists, in the submammary region and on the sides of the neck there had developed moderately well defined groups of slightly pigmented follicular keratotic papules 3 mm. in diameter. A month later (August) a

16. Kren, O.: Lichen ruber spinulosus mit Erkrankung des Capillitiums, abstracted, Zentralbl. f. Haut- u. Geschlechtskr. **59**:369, 1938.

17. Jonquières, E. J.: Peripilarer Lichen planus, abstracted, Zentralbl. f. Haut- u. Geschlechtskr. **59**:482, 1938.

18. Bacciero, V.: Lichen ruber planus case elementi figurati minimi del tranco e contemporanea alopecia a tyso di pseudoarea di Brocq, abstracted, Zentralbl. f. Haut- u. Geschlechtskr. **57**:181, 1938.

biopsy specimen was taken from an area on the right wrist. The patient was not seen again until March 1939. The acuminate papules on the wrists and sides of the neck had undergone involution, leaving a faint pigmentation without evidence of atrophy. The lichen planus was still active on the lower part of the back and in the submammary region. She complained of itching of the vulva, and on the inner surfaces of the labia majora and on the labia minora there was reticulated leukoplakia, typical of lichen planus on the mucous membranes. On the vertex of the scalp there was an area of alopecia, 2 cm. in diameter. The skin was erythematous and atrophic, and on the periphery the follicles were dilated and showed some plugging.

Histologic sections of material from a lesion on the wrist showed only mild hyperkeratosis. In the cutis there was a moderate amount of perivascular infiltrate, which consisted mostly of mononuclear leukocytes and an occasional fibroblast. The striking feature was a large dilated follicle containing a keratotic plug. The specimen had been mounted in such a manner that the follicle had been cut on an angle, and at each pole there was a round or oval well defined band of infiltrate, consisting of numerous mononuclear lymphocytes, a few epithelioid cells and fibroblasts. The infiltrate encroached on the lower layers of the epidermis. The elastic tissue was slightly fragmented and showed a basophilic tint with hematoxylin and eosin stain. These changes, however, may have been within normal limits, according to the patient's age and the location of the lesion.

Case 3.—L. K., a white woman aged 35, was first seen in April 1940, complaining of loss of hair on the scalp. She stated that the onset was in 1937, with generalized eruption. At first the areas of alopecia had enlarged rapidly for a few months, but after that there had been little or no extension. Previous treatment had consisted of ultraviolet radiation and external applications, with no apparent beneficial results.

On the scalp there were well defined, discrete and confluent bald areas 1 to 2 cm. in diameter, some of which were in streaks or rows, such as are seen in "the alopecia serrata of Crocker."[19] The skin in the involved areas was smooth, atrophic and slightly depressed; it was of normal color or light pink, and no dilated capillaries were present.

On the trunk and extremities there was diffuse keratosis pilaris of mild degree. This was especially prominent on the lower or middle part of the abdomen and on the thighs. In addition to these follicular, slightly inflamed, conical papules, measuring 2 to 3 mm., there were approximately a dozen discrete papules which were similar in size and contained deep dark brown or black central plugs, 1 to 2 mm. in diameter. An area including three of the latter plugged papules was removed for microscopic study.

Diseases in the patient's past history included diphtheria, scarlet fever, pneumonia, tonsillitis and an abscess of the abdominal wall. Recently she had had purulent otitis for three years and a trichomonas infection of the genital tract of one year's duration. The important physical findings were perforation of the left ear drum and dermatitis of the external auditory canal. The vaginal mucosa was red in many areas, and a large amount of foamy mucus and pus was seen in the vault of the vagina. The basal metabolic rate was —5 per cent. There was mild microcytic anemia.

Microscopic examination of a specimen from the border of a bald area in the scalp disclosed a definite decrease in the hair follicles. There was no hyperkera-

19. Crocker, H. R.: Diseases of the Skin, London, H. K. Lewis, 1905, p. 1160.

tosis. In some areas the epidermis was atrophic. Many prickle cells had undergone vacuolation leaving deeply stained pyknotic nuclei, which were usually displaced peripherally. There was moderate edema of the basal layer, but there were no exudative cells in the epidermis. In the corium there were some small areas of perivascular infiltration and a few chromatophores and fibroblasts. Occasional hair follicles were replaced by keratotic plugs, and parts of the follicles were surrounded by dense bands of infiltrate, composed mainly of lymphocytes with a few epithelioid cells. These extended to or slightly into the outer layers of the follicles and were usually either at the level of the neck of the follicles or around the tip. The collagen was paler than normal and somewhat sclerotic. There were a few large dilated capillaries in the upper portions of the cutis, and there was an absence of smooth muscles and sweat glands.

The histologic findings may be summarized as follows: early mild atrophy of the epidermis, replacement of hair shafts by horny plugs, well defined bands of cellular infiltration closely surrounding certain parts of the altered follicles, dilated capillaries, increased fibroblasts, sclerotic collagen and destruction of the cutaneous appendages.

Microscopic examination of the biopsy specimen containing the three minute plugged keratotic papules showed under lower power normal epidermis and mild edema of the corium. The striking features were the dilated follicles containing layers of keratotic material. Surrounding the follicles, especially at their lower ends, there was usually a well defined zone of infiltrate consisting principally of lymphocytes with occasional plasma and epithelioid cells. No polymorphonuclear leukocytes were seen. In many areas the infiltrate was localized closely against or extended into the outer layer of cells of the follicles.

COMMENT

Case 1 illustrates a rather common variant of lichen planus: acuminate plugged papules associated with areas of hyperpigmentation, occasionally with slight atrophy and infrequently with decided atrophy, such as that which characterizes the lesion of lichen sclerosus et atrophicans.[19a] Case 2 carries the syndrome a step further. In this patient with typical lichen planus with hyperpigmentation there developed horny plugged acuminate papules and later well defined areas of atrophic scarring in the scalp with dilated and plugged follicular orifices at the borders. Case 3 presented a clinical diagnostic problem. For three years the patient had a lesion of the scalp which was typical of pseudopelade. Histologic examination of tissue from the border of an atrophic area showed dilated follicles with horny plugs and well defined bands of lymphocytic infiltration closely packed around the lower ends of the follicles. We believe that this type of sharply localized perifollicular infiltration associated with a dilated follicle containing a horny plug to be suggestive of lichen planus et acuminatus. Microscopic examination

19a. We agree with Montgomery and Hill that lichen sclerosis et atrophicans is not the same as atrophic lichen planus (Montgomery, H., and Hill, W. R.: Lichen Sclerosus et Atrophicus, Arch. Dermat. & Syph. **42**:755 [Nov.] 1940).

of tissue from the acuminate lesions on the body also showed zones of cellular infiltration in juxtaposition to the modified basal layer of the follicle, with a few exudative cells penetrating beyond and into the outer layer of prickle cells.

The histologic changes apparently are identical with those observed by McCafferty [9] and Feldman.[2] In keratosis pilaris and lichen spinulosus the infiltrate is more diffuse and does not form well defined zones or bands around the follicles. The infiltrate in the cases herein reported

An acuminate lesion with a keratotic follicular plug and a well defined band of lymphocytes at the end of the follicle, with slight extension of the infiltrative cells into the outer rows of rete cells.

penetrated the outer layers of rete cells of the follicles in a manner analogous to that seen in the common lichen planus papule.

DIFFERENTIAL DIAGNOSIS

In considering the differential diagnosis the following questions should be posed: Are folliculitis decalvans and pseudopelade variants of the same disease? Are they separate disease entities or are they simply clinical syndromes which may arise from various etiologic factors?

Savill [20] described folliculitis decalvans, pseudopelade and lichen planus et acuminatus atrophicans separately but grouped all three under one heading when their therapy was considered. McCarthy [21] separated folliculitis decalvans and pseudopelade. In addition, he cited a case of lichen planus atrophicus et sclerosus (lichen albus of von Zumbusch) involving the scalp. He obtained three biopsy specimens; examination of two showed changes suggestive of lichen planus, while the third was typical of the atrophic stage. McCarthy [22] stated that cases classified under the title of folliculitis decalvans et atrophicans are probably true instances of folliculitis decalvans and that the finding of lichen spinulosus on the body and folliculitis decalvans on the scalp is just another example of a coincidental relation that occurs frequently in dermatology. Such lesions, he stated, should be reported as two separate diseases and not as a new clinical entity composed of already known elementary diseases. Feldman stated: "I consider follicular plugging and follicular dilatation of such importance that I am ready to make a diagnosis of atrophic lichen planus on the basis of those symptoms if they are found simultaneously with atrophy." He contended that he has seen atrophy extend in advance of or precede the infiltrate of lichen planus.

The acuminate papules on the body are generally differentiated with ease from papules seen in pityriasis rubra pilaris, lichen spinulosus and keratosis pilaris. Sutton and Sutton [23] made the statement that Feldman "indicated that lichen spinulosus is a form of lichen planus." Our interpretation of Feldman's view is that he considered the so-called lichen spinulosus, as associated with the syndrome under consideration, as not being lichen spinulosus but acuminate lichen planus papules. The diagnosis of lupus erythematosus, favus and folliculitis decalvans are not difficult to exclude if the active lesion is present. However, when the lesion is of long duration, inactive or atypical, the alopecia and scarring may be mistaken for that which may accompany lichen planus et acuminatus atrophicans.

SUMMARY

Feldman interpreted the syndrome of folliculitis decalvans et lichen spinulosus of Graham Little as a form of atrophic lichen planus associated with acuminate papules. He described the disease under the title of lichen planus et acuminatus atrophicans.

20. Savill, A.: The Hair and Scalp, Baltimore, William Wood & Company, 1935, p. 133.

21. McCarthy,[8] p. 559.

22. McCarthy,[8] p. 279.

23. Sutton, R. L., and Sutton, R. L., Jr.: Diseases of the Skin, St. Louis, C. V. Mosby Company, 1939, p. 320.

Certain features of the 3 cases herein reported lend support to Feldman's views. In 2 of the cases, in which there apparently was pseudopelade, there were acuminate lichen planus papules.

The histologic finding of a well defined lymphocytic cellular infiltration at the lower pole of a dilated follicle containing a keratotic plug is characteristic of the lesion of lichen planus et acuminatus.

The various forms of atrophic lichen planus and closely related clinical syndromes need further elucidation.

8 East Madison Street.

1610 Twentieth Street, North West.

LATE, OR DELAYED, REACTIONS TO PATCH TESTS

GEORGE V. KULCHAR, M.D.
SAN FRANCISCO

In the determination of the numerous causes of contact dermatitis of the eczematous type, the patch test has been of almost immeasurable aid. In approximately one third of the patients in whom the cause is not immediately apparent, the etiologic agent can be discovered by patch testing. Increasing experience has so conclusively demonstrated the value of the method that its use has become almost routine in the management of dermatitis of the contact-eczematous type. General acceptance of the patch test has given to it a measure of legal standing in industrial dermatology, in which the method has found its widest application. If this is to continue, further study directed particularly to the mechanism and the cyclic variations in the responses to patch tests is necessary. Likewise greater recognition of the possibility of late, or delayed, reactions, with an understanding of the factors underlying them is desirable.

Although delayed reactions have been reported (Sulzberger,[1] Ingram [2] and Cavendish [3]), little attention usually is given to them in routine practice. Certain substances, such as trichophytin and poison ivy extract, seem peculiarly disposed to cause delayed reactions in patch tests, according to Sulzberger. That the delayed reactions may be due to sensitization induced by the patch test itself, since they are more frequently observed in persons in whose cases there has been no likelihood of previous contact with the materials tested, has been suggested by Cavendish. Sensitization by means of repeated patch tests has been reported by Beerman.[4] The studies of Ingram have shown conclusively that delayed reactions are frequently encountered among patients not

From the Division of Dermatology and Syphilology, Department of Medicine, Stanford University School of Medicine.

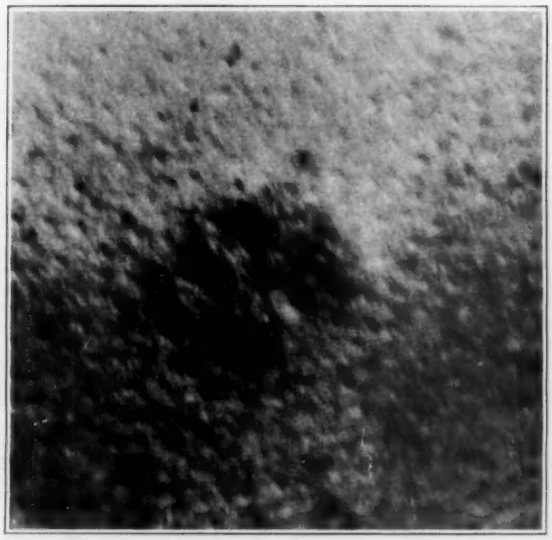
1. Sulzberger, M. B.: Dermatologic Allergy, Springfield, Ill., Charles C. Thomas, Publisher, 1940, p. 123.

2. Ingram, N. T.: Dye Dermatitis in Relation to Idiosyncrasy, Brit. J. Dermat. **44**:422 (Aug.-Sept.) 1932.

3. Cavendish, A.: A Case of Dermatitis from 9-Bromo-Fluorene and a Peculiar Reaction to a Patch-Test, Brit. J. Dermat. **52**:155 (May) 1940.

4. Beerman, H.: The Patch Test in Determination of Arsphenamine Sensitization, Pennsylvania M. J. **39**:690 (June) 1936.

previously sensitized. Patch tests with metaphenylenediamine and paraphenylenediamine made on 1,000 patients who previously had manifested no evidence of sensitivity to these dyes resulted in 27 delayed reactions. While the majority showed positive reactions in less than two weeks, latent periods up to twenty-four days were observed. The delayed reactions were probably due, according to Ingram, to sensitization induced by the patch test. Once sensitization has been established, the reaction time is remarkably constant at twenty-four to forty-eight hours (Sulzberger). During or immediately after the subsidence of acute dermatitis, however, there may be occasionally a temporary period of refractoriness.



Delayed reaction to patch test made with nupercaine ointment, appearing forty-five days after application in a patient with dermatitis due to sensitivity to nupercaine.

A delayed reaction of forty-five days to a patch test made with a 1 per cent nupercaine ointment on a patient with an eczematous dermatitis due to sensitivity to nupercaine prompted a further study, in the hope that some causal factor might be elicited to explain the prolonged refractory period.

REPORT OF A CASE

Mrs. L., aged 64, in June of 1938 received 4,800 r of low voltage, unfiltered roentgen rays in the treatment of a basal cell epithelioma in the region of the outer canthus of the right eye. The lesion underwent involution, and epithelization occurred. After this the patient disappeared from observation but returned in September 1939 complaining of severe pruritus in the area irradiated, at which time erythema, scaling and a slight amount of atrophy were noted, and the diag-

nosis of late roentgen ray dermatitis was made. An ointment containing 1 per cent nupercaine in petrolatum was prescribed. On the day after the initial application of the ointment acute vesicular dermatitis appeared over the entire upper half of the right cheek. Patch tests were made with both nupercaine ointment and petrolatum. These reactions were negative at the end of forty-eight and seventy-two hours, and with the use of wet dressings and emollients the dermatitis disappeared in about twelve days. Because a delayed reaction to nupercaine was suspected the patient returned at frequent intervals during the ensuing four weeks, during which time no evidence of reaction could be observed. A definite positive reaction of the eczematoid type (figure) appeared at the site of the patch test made with nupercaine ointment forty-five days after its application. The reaction persisted for eleven days and was not accompanied by any flare-up in the region involved by the dermatitis. During the interim, so far as could be ascertained, there had been no contact with nupercaine in any form. Inquiry revealed no

Summary of the Results of Patch Tests with One Per Cent Nupercaine Ointment on the Same Patient over Eight Months

Patch Test Number	Date	Site of Application	Days Elapsing Before Positive Reactions Appeared	Reaction
1	10/ 2/39	Right arm	45	Positive
2	11/24/39	Left arm	4	Positive
3	11/29/39	Right arm	9	Positive
4	12/ 5/39	Left arm	8	Positive
5	12/11/39	Right arm	6	Positive
6	12/18/39	Right thigh	..	Negative
7	12/27/39	Right arm	7	Positive
8	1/ 4/40	Left thigh	8	Positive
9	2/15/40	Left arm	11	Positive
10	3/ 4/40	Right arm	5	Positive
11	3/10/40	Left arm	4	Positive
12	3/18/40	Right arm	3	Positive
13	4/ 1/40	Right arm	4	Positive
14	4/ 8/40	Back	4	Positive
15	4/18/40	Left arm	5	Positive
16	7/18/40	Right arm	2	Positive

history of atopy or previous dermatoses. Nupercaine or its related compounds had not been used on the skin, although procaine hydrochloride had been employed previously for dental anesthesia.

The method of performing the patch test is too well known to require a detailed description. In practice the reactions are usually read at the end of forty-eight hours and occasionally again at seventy-two hours. If a positive reaction is not observed by this time, the substances tested are generally eliminated as being the cause of the dermatitis.

In the case reported, during the subsequent nine months fifteen patch tests with the same ointment were made on various areas on the patient's body. Care was taken to insure a homogeneous distribution of the nupercaine in the base by thorough mixing. The patches were removed after forty-eight hours and the reactions read by the same observer in each instance. Control tests made with petrolatum repeatedly gave negative results. The results are summarized in the table.

The initial patch test made at the time the dermatitis first appeared showed no reaction until forty-five days later, at which time an eczematoid reaction, sharply localized to the area of application, was noted. No evidence of reaction prior to the forty-fifth day could be observed, although the site had been examined repeatedly. Subsequent to the onset of the dermatitis nupercaine in any form had not been used. The delayed reaction may well have been due to a "refractory phase" induced by the dermatitis, sufficient nupercaine having remained fixed in situ to produce a positive reaction after subsidence of the "refractory phase." Similar refractory periods during or following dermatitis of the eczematous-contact type have been reported by Sulzberger.

Although one of the patch tests (no. 7) never elicited a positive reaction during the seven month period of observation, the reaction time tended to become shorter with repetition of the tests. The last test made (no. 16) showed a positive reaction at the end of forty-eight hours (the usual period). No significant change in the degree of reaction could be observed. The trend of the reaction time to become less with the repetition of the tests suggests that the sensitivity was increased by this means. It has not been established, however, that the reaction time is an index of the degree of sensitivity, although a positive reaction usually appears more rapidly in persons with decided sensitivity. Delayed reactions to patch tests (beyond forty-eight hours) usually occur, according to Cavendish, when no sensitivity exists except for that induced by the test itself. The evidence for this is based largely on the observation that delayed reactions are observed with greater frequency among persons in whom there is no history of previous contact with the substance tested.

The reason for the repeatedly delayed reactions elicited in the patient reported on here cannot be definitely stated. The differences in the reaction time cannot be explained on the basis of regional variations in sensitivity, since they were encountered in all the areas tested. Several other explanations suggest themselves. As Sulzberger has stated, "Many allergic processes, including contact dermatitis, seem to present kaleidoscopic phases of hypersensitivity, of lesser sensitivity and normal degrees of sensitivity." As yet no cause for these variations has been discovered, although some unknown or "constitutional factor" is usually predicated. Commonly, as in the case reported here, no reason can be found to account for the cyclic variations observed.

If the reaction time is interpreted as a measure of sensitivity, the decreases noted with the successive repetition of the patch tests suggest that the degree of sensitization was increased by this means. It must be assumed, then, that the original degree of sensitivity was regional and relatively slight, although sufficient to produce dermatitis in an

area previously injured by roentgen rays. The differences in the reaction time observed in patch tests made with nupercaine may well be due to cyclic variations in this sensitivity, modified by the increasing sensitization induced by the repeated patch tests.

SUMMARY

A delayed reaction, appearing only after forty-five days, to a patch test with nupercaine ointment on a patient with a dermatitis due to sensitivity to nupercaine is reported. Similar tests made subsequently showed repeated delayed reactions with a tendency toward a decrease in the reaction time with repetition, suggesting an increasing sensitivity induced by the test. Some of the factors seemingly concerned in the variation in the reaction time are discussed.

In view of the emphasis that has been placed on the patch test in the search for causes of eczematous-contact dermatitis, it is suggested that more attention and recognition be given to delayed positive reactions.

ROLE OF EVOLUTION IN DERMATOLOGY

CHARLES LERNER, M.D.
NEW YORK

The gulf that divides medicine, in practice, from biology has often been deplored. Modern biologic research compels the physician to free himself occasionally from the traditional medical viewpoint of disease and consider his problems afresh from the biologic approach.

The dermatologist, especially, can gain new light by a study of the manner in which the human skin and its appendages have developed (both ontogenetically and phylogenetically), the factors which promote or inhibit their growth and the development of disease-producing agents, such as bacteria—in other words, the evolutionary process in its relation to the etiology of diseases of the skin. This paper will, therefore, be limited to an attempted clarification of the role of evolution in dermatology.

It is known that the human embryo begins its development after fertilization by the division of a single cell, outwardly similar to the process of fission by protozoa. This single cell eventually gives rise to all the tissues of the body, with their varying degrees of differentiation. The question of whether the mature body cells can retain or revert to this omnipotentiality is important in the consideration of abnormal cell reproduction.

A brief review of the chronologic development of the human skin and its appendages in embryo may throw light on the manner in which a "lag" or an undue acceleration in the development of one part due to abnormalities in the embryonic environment (e. g., defective or excessive hormonal secretions) may lay the foundation for future pathologic manifestations or responses to adult stimuli. The production of embryonic folds due to unequal rates of growth is an essential factor in the formation of all organs of the body and hence controls, to a large extent, the general form.

The earliest differentiation in the embryo is that between ectoderm and endoderm, which gives rise to the mesoderm. The skin, its appendages and the nervous system develop from the ectoderm; the connective tissue and the skeletal and muscular systems, from the mesoderm, and the other internal organs, from the endoderm. The endoderm normally has no part in the development of the skin, although the possibility of the development of endodermal tissues from epidermal cells seems to

have been demonstrated experimentally (Nusbaum and Oxner,[1] Huxley [2] and Child [3]).

Modern knowledge of the principles of ontogenetic development is summarized in the laws of von Baer. The development from one stage of the ontogeny to the next has been shown to be influenced by the genes not only qualitatively but also by modifications in their comparative rates of growth. Since most animals go through no further ontogenetic stages after reaching sexual maturity, it will be seen that variations in the rate of development of the genes controlling the sex characters may serve to prevent or to permit the development of the other characters. De Beer [4] pointed out that such an arrest of development, known as neotony, may have taken place in the evolution of some animals and cited permanently neotonous forms, such as some of the newts. Similarly, a retardation of development may result from the delaying of sexual maturity (as is shown by the progressively delayed appearance and reduced quantity of hair in monkeys, apes and man), so that a formerly embryonic characteristic eventually becomes an adult one. An extreme form of this process, perhaps, is seen in congenital ectodermal defect. The frequent association of hypertrichosis with precocious puberty or with the menopause suggests that this condition may also be classed among the examples of neotonous characteristics.

In addition to variations, often self perpetuating, produced by the process of neotony, there are others which are due primarily to the presence of a new stimulus or inhibitor or to the reproduction of some feature of the ancestral environment, whether external, e. g., change of position of the embryo, or internal, e. g., endocrine changes. Such reversion to the ancestral environment accounts for the characters termed atavisms.

The pigmented nevi have been cited by Laidlaw and Murray [5] (I [6] also have previously stressed this point) as a possible instance of

1. Nusbaum, J., and Oxner, M.: Studien über die Regeneration der Nemertinen, Arch. f. Entwcklngsmechn. d. Organ. **30**:74, 1910.

2. Huxley, J. S.: Time Relations in Amphibian Metamorphosis, Science Progr. **17**:606, 1923; Constant Differential Growth-Rates and Their Significance, Nature, London **114**:895, 1924; Further Studies on Restitution Bodies, Quart. J. Micr. Sc. **65**:293, 1921; The Individual in the Animal Kingdom, New York, The Macmillan Company, 1912.

3. Child, C. M.: Senesence and Rejuvenation, Chicago, University of Chicago Press, 1915; Physiological Foundations of Behavior, New York, Henry Holt & Company, 1924.

4. De Beer, G. R.: Embryology and Evolution, New York, Oxford University Press, 1930.

5. Laidlaw, E. F., and Murray, M. R.: Theory of Pigmented Moles, Am. J. Path. **9**:827, 1933; **10**:13, 1934.

6. Lerner, C.: Etiology of Nevi, Urol. & Cutan. Rev. **40**:185, 1936.

atavism. They pointed out that all tumors show a resemblance to some normal structure and showed the close histologic similarity of the pigmented moles and the tactile hairs of rodents and carniverous animals and the pigmented tactile spots on certain fish. This atavistic theory of the causation of pigmented nevi might also throw light on the systematized forms. Masson's [7] work, although disputed by some observers, convinced him that nevus cells were derived from dendritic and tactile cells.

Atavism may also furnish an explanation for many of the common anomalies of hair, nails and pigment and for conditions such as ichthyosis. If the latter is truly an atavism, presumably the skin, at least in embryo, has in every human being the capability of reacting in this manner, although in only a few is this response actualized by the appropriate stimulus. It will be recalled that in the extreme form of ichthyosis the fetus is usually a nonviable monstrosity, with fingers and toes resembling talons and claws. Cases of ichthyosis have also been reported in which there were associated disorders or malformations of the cutaneous glands and lack of hair. It is interesting to note that various endocrine disturbances have been frequently found in cases of ichthyosis. Cutis hyperelastica is another condition familiar to the dermatologist which may be considered an atavism; the resemblance of the skin in this condition to that of the young of some of the lower animals (cats and dogs) has often been noted.

The various keratotic dermatoses also appear to be partially atavistic in character. Frank,[8] Sligh,[9] Stone [10] and others have reported cases in which the entire integument was regularly shed like that of a serpent. An interesting form of keratoderma is the so-called mal de Meleda, in which the congenital keratosis of the palms and soles is associated with an ichthyotic thickening of the wrists and ankles; the condition has been attributed by some observers in part to intermarriage.

Another class of variations modifying the phylum is the so-called adaptation. The old teleologic notion that an organism is able to "adapt" itself to changes in its environment by structural modifications designed to favor its survival has largely given way to the concept that the body adapts its function so as to use the environmental modifications except when the change is a simple chemical reaction. Perpetuated variations

7. Masson, P.: Les nævi pigmentaires, tumeurs nerveuses, Ann. d'anat. path. **3**:417, 1926.

8. Frank, J.: A Remarkable Case of Skin Disease, Am. J. M. Sc. **102**: 164, 1891.

9. Sligh, J. M.: A Unique Case of Annual Shedding of the Epidermis, Internat. M. Mag. **2**:463, 1893.

10. Stone, R. M.: Keratolysis or "Skin Shedding," J. A. M. A. **35**:557 (Sept. 1) 1900.

may thus be regarded as overcome diseases. An obvious example of this is seen in the formation of calluses, which becomes a necessary or useful "adaptation" in many occupations.

The most important single factor in embryonic development, and the most controversial, is that of heredity. Some experiments have seemed to prove conclusively that so-called acquired variations can be transmitted to later generations; other observations demonstrate at least a possibility that, as Child [3] claimed, internal or inherited factors merely enable the organisms to react in definite ways to external stimuli, so that heredity does not account for the whole person but determines only certain potentialities, some of which may be realized in the person. It is probably safe to conclude that "no single part is completely acquired or due to inheritance alone" (Goodrich [11]). Experimental evidence has shown, the same investigators and others have pointed out, that characters which originally arose as responses must be called forth anew in every generation. Such hereditary potentialities are seen, for example, in xeroderma pigmentosum, in which exposure to light or sun is necessary to activate the inherited predisposition of the skin to malignant growth. Hereditary characters are transmitted through the individual cells, and the cells may retain their early plenipotentiality.

All of the physiologic growth factors considered here, which have played such an important role in evolutionary development, are of obvious significance in a consideration of pathologic or neoplastic growth. These factors may be grouped under the general headings of normal cell differentiation, inducers or organizers of growth and inhibitors of growth.

It is well known that the process of cell differentiation is one of gradual death, so that as cells differentiate and become functional they lose their powers of reproduction. Thus only a comparatively undifferentiated cell can proliferate. It is on this principle that Broders [12] established his degrees of malignancy, based on the proportion of differentiated to undifferentiated cells in a new growth. The energy of a cell must be utilized either for proliferation or for differentiation (usually functional) and cannot be used for both. Moreover, the expenditure of this energy for either process is necessarily attended by structural changes in the cell. The diversion of energy to proliferation constitutes malignancy. Hence the more highly differentiated a cell, the less likely it is to proliferate, and the tissues in which the cellular elements exhibit frequent mitosis are the most likely to proliferate excessively and show tumor growth.

---

11. Goodrich, E. S.: Living Organisms, New York, Oxford University Press, 1924.

12. Broders, A. C.: Practical Points on the Microscopic Grading of Carcinoma, New York State J. Med. **32**:667, 1932.

The establishment and development of the embryo in the uterus present a most interesting illustration of this principle. The human ovum at one week has already eroded the uterine mucosa through the epithelium to the capillaries at the spot where the "invasion" is arrested, and differentiation of the embryo begins (Peters [13]). The syncytial cells, if they are not expelled in labor or if death of the fetus intervenes to arrest functional development, may continue and extend the invasive process and even send out metastases, becoming malignant syncytiomas or chorion epitheliomas. It is interesting to note here that the work of Shaw-Mackenzie [14] demonstrated the role that the fatty acids and lipolytic enzymes play in tissue immunity and showed that fetuses, pregnant women and patients with carcinoma are all low in lipolytic factors.

It is well known that slight injury—for example, a needle prick—can start the division of the egg in parthenogenetic organisms, and recent experiments seem to show that this response can be similarly obtained in higher animals as well. It thus appears that embryonic growth, malignant growth and regenerative growth may be comparable, at least in origin.

Experimental evidence points to the existence of certain organizers of growth which direct, in a sense, the type of development. Experiments have shown that the inductive power is present even in nonliving material and hence is probably a chemical reaction (De Beer [4]).

The possibility that some or all of the cells of the body may retain their early omnipotentiality is of special importance in dealing with new growths, benign or malignant. Definite work has still to be done on the problem of inheritance of cancer; but physicians would do well at least to bear in mind the extent of the inherited or innate potentialities of the individual cells, some of which may be realized when morbid cell reproduction is unchecked. The frequent reports of what have been termed transitional cell carcinomas, in which the tumor appears to be composed of both basal and prickle cells or of cells with characteristics of both, and the controversy as to whether a basal cell carcinoma can develop into the more malignant prickle cell type are especially significant from this point of view. Histologically, melanoma is also a manifestation of cell potentialities not realized in normal growth, and it is interesting to note here the observations of the so-called basal cell epitheliomas

13. Peters, H.: Ueber die Die Einbettung des menschlichen Eies, Leipzig, Franz Deuticke, 1899.

14. Shaw-Mackenzie, J. A.: The Mechanism of Immunization, Lancet **2**:825, 1919; Some Reactions of the Blood After Cancer Inoculation, Tr. Internat. Cong. Med., London (1913), 1914, sect. 5, pt. 2, p. 295.

containing melanin, which are nevertheless distinct histologically from the typical melanoma (Eller and Anderson [15]).

The sex hormones appear to play an important role in both physiologic and pathologic growth, probably as inhibitors of growth. The effect of sexual maturity on development has already been mentioned. Apparently the sex-controlling genes, or the secretions of the structures produced by them, exert a mutually inhibiting effect, so that the functioning of the female sex organs tends to prevent the development of male ones, and vice versa. This natural inhibition is strikingly demonstrated by the sexual structure and development of female birds, which are equipped with both functioning ovaries and undeveloped testicles and in which the testicles continue their previously arrested development if the ovaries are removed.

The relation of the sex hormones to growth is a field that has hardly been investigated, but interesting fields of speculation and future lines of therapy are opened by consideration of such facts as the effect of some tumors on sexual characters (e. g., gynecomastia), the frequency of mammary and uterine tumors, the increased growth of and susceptibility to tumors at the menopause and the relation of many minor dermatoses (such as acne, dermatitis dysmenorrhoeica and herpes progenitalis) to the sexual cycle. The possibility of the development of a natural inhibition against the growth of tumors might even cause their differentiation into new functional organs in the evolutionary process, repeating the cycle of a disease perpetuated as a structural modification.

It is perhaps of some significance that endocrine secretions of a sort are found even in the lowest forms of life, in which they apparently enable an organism to sense danger and react to it. It has recently been found that when the surface of a plant is cut it secretes a hormone which has a definite healing action on the injured tissues. It will be recalled that malignant growth, which represents from one point of view a failure of the organism to react or adapt itself to injury, is also found throughout nature, unlike most human diseases.

It is possible that the relation of the endocrine glands to both normal and abnormal or malignant growth and function indicates one of the mechanisms by which evolutionary modifications have been brought about. Modern investigation has shown some of the many ways in which the endocrine secretions may be influenced by the external environment; and the apparent relation between hormones and vitamins, although as yet incompletely investigated, offers a clue as to how even the food one eats may affect the internal secretions that govern the nervous system and indirectly the structure and function of all the organs,

15. Eller, J. J., and Anderson, N. P.: Basal-Cell Epithelioma with Excessive Pigment Formation, Arch. Dermat. & Syph. **27**:277 (Feb.) 1933.

with consequent perpetuated variations. Thus modifications in pigment originally caused by climate may be perpetuated by concomitant endocrine changes. The special forms of chloasma occurring in pregnancy and at adolescence may offer a clue here, as may acanthosis nigricans, the adult type of which seems always to be associated with internal cancer and the juvenile type with endocrine dysfunction. The alterations in pigment so frequently associated with myxedema may also be of significance on this point.

Moreover, it seems likely that it is through such changes in the endocrine secretions that so-called "acquired" characteristics may be passed on to future generations, since such changes constitute a change in the embryonic environment that may call forth similar modifications. It would be particularly interesting to study more closely the role of the hormones in such a condition as epidermolysis bullosa hereditaria, which may well have originated because of an inability to become adapted to the loss of the protective covering of the hair (which may "anchor" the skin as well as shield it), resulting in skin in which the defensive powers are too weak to resist even the slightest trauma. It is well known that epidermolysis bullosa often subsides spontaneously at puberty. Guy [16] found a persistent thymus in some of his cases, and Beinhauer [17] in recent years has reported good results from endocrine therapy in epidermolysis bullosa.

A similar mechanism may be active in the causation of hyperhidrosis and seems especially likely in view of the frequency of occurrence of this condition at adolescence and the menopause and in connection with disturbances of the thyroid and other glands. On the palms and soles, especially, hyperhidrosis may well represent a throwback to an earlier evolutionary "adaptation" or reaction to the presence of danger, by which the animal was enabled more easily to grasp things or to climb a tree to safety. The absence of sebaceous glands on the palms and soles would tend, in my opinion, to substantiate this consideration, because a mixture of sebum and sweat on the hands and feet would prove disastrous in climbing a tree. Viewed in this light, such a hyperfunction might be considered rather as a natural reaction or defense, and any attempt to check it artificially might even lead to a reversion from function to proliferation. Keratosis, also found frequently on the palms and soles, may be parallel to this process, representing a reaction to injury, invasion or other stimulus by overgrowth, which is usually eventually arrested. This would throw further light on the frequency

16. Guy, W. H.: Epidermolysis Bullosa, Arch. Dermat. & Syph. **15**:30 (Jan.) 1927.

17. Beinhauer, L. G.: Treatment of Epidermolysis Bullosa, Arch. Dermat. & Syph. **32**:469 (Sept.) 1935.

with which keratoses become cancerous. Keratosis would then represent the opposite tendency to epidermolysis bullosa.

On the other hand, one must consider the possible evolutionary changes in the external disease-producing agents and in defenses of the body (acquired immunity).

The mysterious disappearance of some common ancient plagues and the apparently sudden beginning of certain modern ones have often been remarked. Thus tuberculosis is unmistakable in the earliest Greek writings, and leprosy is described in the 12,000 year old Papyrus Ebers; but Smith [18] found no traces of syphilitic osteitis in the 10,000 skeletons taken from ancient Egyptian burying grounds. This would seem to indicate a certain evolutionary progress in disease-producing agents, such as bacteria, or in the ability of the human organism to withstand them, or in both.

It has been proved experimentally (Thiele and Embleton [19]) that saprophytic bacteria can be induced to evolve, by changes in their environment, into pathogenic ones—e. g., Bacillus mycoides has developed, under controlled environmental changes, into Bacillus anthracis. These experiments have shown that bacteria, like animals and other plants, can be modified by their environment, that an alteration in the environment leads inevitably to a particular alteration of form or function and that such modifications cannot possibly be "chance variations" with a survival value, since all the subjects react with the same variation to the same environmental alteration. The work of Faber [20] along these lines has cast new light on the possible relation of rapid bacterial evolution to the phenomena of anaphylaxis.

It is apparent that the immunizing reactions of the body have also played an important role in the historical evolution of disease. Since, as mentioned earlier, the tissues and organs overcome invading bacteria or cells by making use of them for growth or construction, acquired immunities must eventually produce modifications of form and function. Thus the allergic phenomena which are so important in dermatology may be seen, in a sense, as adaptations which may represent a further step in the evolutionary process.

On the other hand, as Lockhart-Mummery [21] has pointed out, evolution may work in a downward as well as an upward direction, and it

---

18. Smith, G. E.: Syphilis in Prehistoric Egyptians, Lancet **2**:1788, 1907; **2**:521, 1908.

19. Thiele, F. H., and Embleton, D.: Pathogenicity and Virulence of Bacteria, Ztschr. f. Immunitätsforsch. u. exper. Therap. **19**:643, 1913.

20. Faber, H. K.: Experimental Arthritis in the Rabbit, J. Exper. Med. **22**: 615, 1915.

21. Lockhart-Mummery, J. P.: Evolution and Disease, Proc. Roy. Soc. Med. **29**:1234, 1936.

may well be that the simpler-functioning organisms, such as the bacteria, represent a more perfect evolutionary development than the complex and uneconomical form. Certainly the bacteria and the viruses of human disease are a later development than man, their host, and their survival value, evidenced particularly in reproductive speed and adaptive power, is enormously greater. Thus it seems unlikely that man can develop permanent immunities faster than the disease-producing agents can evolve to overcome these immunizing reactions.

It must be remembered, too, that man is still evolving, as seen, for example, in the progressive tendency to degeneration and loss of teeth and hair; and his evolution has brought about not only new immunities but new dangers and predispositions to disease as well. Thus the periods of infancy, childhood and senility—the most dangerous to any organism—have been and are still being gradually prolonged in man; the assumption of the erect posture has adversely affected the circulation and brought about modifications of the pelvic and abdominal organs; the greater slenderness of the bones has made them more susceptible to injury, and the tendency to greater delicacy of the skin has made it less resistant to exposure. This evolutionary course of the human species, if continued, will place mankind at an even greater disadvantage beside the agents of disease.

It has been the purpose of this paper to point out some of the relations between evolutionary biology and dermatology. The subject is vast, but it is hoped that this tentative sketch will at least serve to suggest certain hypotheses and speculations and perhaps to broaden or clarify some of the dermatologists' bases for etiology and therapy.

152 West Fifty-Eighth Street.

XCI. TATTOO TYPE BLEMISHES FOLLOWING USE OF IRON SALTS IN TREATMENT OF RHUS DERMATITIS

RICHARD S. WEISS, M.D.

ADOLPH H. CONRAD, M.D.

AND

ADOLPH H. CONRAD JR., M.D.

ST. LOUIS

McNair [1] in 1917 recommended the use of iron salts in the treatment and prevention of poison ivy dermatitis. He found a rational explanation of its apparent good effect in that the toxic principle of rhus is precipitated and perhaps denatured when it comes in contact with iron. This method of treatment was first used by White in 1873; [2] therefore, it seems to have been in use for many years previous to McNair's report.

Pusey [3] in 1930 was the first to report a case of brown stains in the skin from wet dressings of a solution of ferrous sulfate. The stains on his patient's skin remained for years. Traub and Tenner [4] reported 2 cases of this type of metallic pigmentation following the use of solutions of ferrous sulfate and ferric chloride and referred to 4 additional cases occurring in the service of Dr. George M. MacKee. Sutton [5] reported a case of this condition following the use of strong solutions of ferrous sulfate and lead acetate. He stated the belief that the iron was precipitated in the skin as the acetate. Foerster [6] stated that he had observed several cases of "tattoo marks" following the use of ferric

---

Studies, observations and reports from the Department of Dermatology of the Barnard Free Skin and Cancer Hospital and from the Department of Dermatology, Washington University School of Medicine, service of Dr. M. F. Engman Sr.

1. McNair, J. B.: A Contribution to the Chemotherapy of Rhus Dermatitis, Arch. Dermat. & Syph. **3**:802-808 (June) 1921; Rhus Dermatitis, Chicago, University of Chicago Press, 1923, p. 179.

2. White, J. C.: On the Action of Rhus Venenata and Rhus Toxicodendron upon the Human Skin, New York M. J. **17**:225-249, 1873.

3. Pusey, W. A.: Brown Stains in Skin from Wet Dressings of a Solution of Copperas, J. A. M. A. **94**:207 (Jan. 18) 1930.

4. Traub, E. F., and Tenner, J. S.: Permanent Pigmentation Following Application of Iron Salts, J. A. M. A. **106**:1711-1712 (May 16) 1936.

5. Sutton, R. L., Jr.: Pigmentation of the Skin Due to Iron (Copperas) Applied Locally, J. A. M. A. **108**:112-113 (Jan. 9) 1937.

6. Foerster, H. A.: The Treatment of Poison Ivy, J. Oklahoma M. A. **31**: 245-247 (July) 1938.

chloride solution and stated the opinion that it should not be used for local treatment. Reyner [7] reported another case of pigmentation following the use of ferrous sulfate. He stated that the pigmentation could be removed with ultraviolet irradiation. His patient had applied buttermilk after using ferrous sulfate.

The use of iron salts has been popularized for the layman in other than academic medical publications. For instance, in *Hygeia* [8] it was stated that a 5 per cent solution of iron chloride is an effective remedy for the treatment of ivy poisoning in its early stages. In a botany leaflet of the Field Museum of Natural History McNair [9] recommended the use of 5 per cent ferric chloride in 50 per cent alcohol as a preventive and as an effective treatment.

In supplement 161 of the *United States Public Health Reports* [10] the use of iron salts was recommended, but it was mentioned that several cases of persistent discoloration had been reported. Practitioners have become acquainted with this method of treatment through textbooks and in the section "Queries and Minor Notes" in *The Journal of the American Medical Association.*[11] Canadian physicians were acquainted with the treatment by Byram,[12] who did not mention the disfigurement which may follow. Without mentioning its disadvantages, McNair [13] recommended the use of iron salts to biology teachers. Manlove [14] has recommended it to Navy medical officers.

REPORT OF A CASE

A 23 year old white woman was first seen at the dermatologic clinic of the Barnard Free Skin and Cancer Hospital on July 8, 1940. She complained of brownish black discoloration on the left side of her face and neck and on both forearms.

On May 28, 1940 the patient had been exposed to poison ivy, and two days later a profuse eruption appeared on her face and arms. She treated the eruption

---

7. Reyner, C. E.: Pigmentation Following the Use of Iron Salts, Arch. Dermat. & Syph. **40**:380-381 (Sept.) 1939.

8. Iron Chloride Solution Is Good Treatment for Poison Ivy, Hygeia **10**:767 (Aug.) 1932.

9. McNair, J. B.: Poison Ivy, Leaflet 12, Botany, Field Museum of Natural History, Chicago, 1926.

10. Ivy and Sumac Poisoning, Pub. Health Rep., 1940, supp. 161.

11. Ivy Poisoning and Lobinol, Queries and Minor Notes, J. A. M. A. **97**: 341 (Aug. 1) 1931. Dermatitis Venenata, Queries and Minor Notes, ibid. **102**: 1517 (May 5) 1934.

12. Byram, A. T.: Poison Ivy Control, Canad. Pub. Health J. **22**:291-292 (June) 1931.

13. McNair, J. B.: A Dependable Remedy for the Poison Ivy Group, Am. Biol. Teacher **2**:100-101, 1940.

14. Manlove, W. L., Jr.: Ivy Poisoning, U. S. Nav. M. Bull. **33**:183-187 (April) 1935.

Fig. 1.—Distribution of tattoo type blemishes on the face and neck and on the forearms.

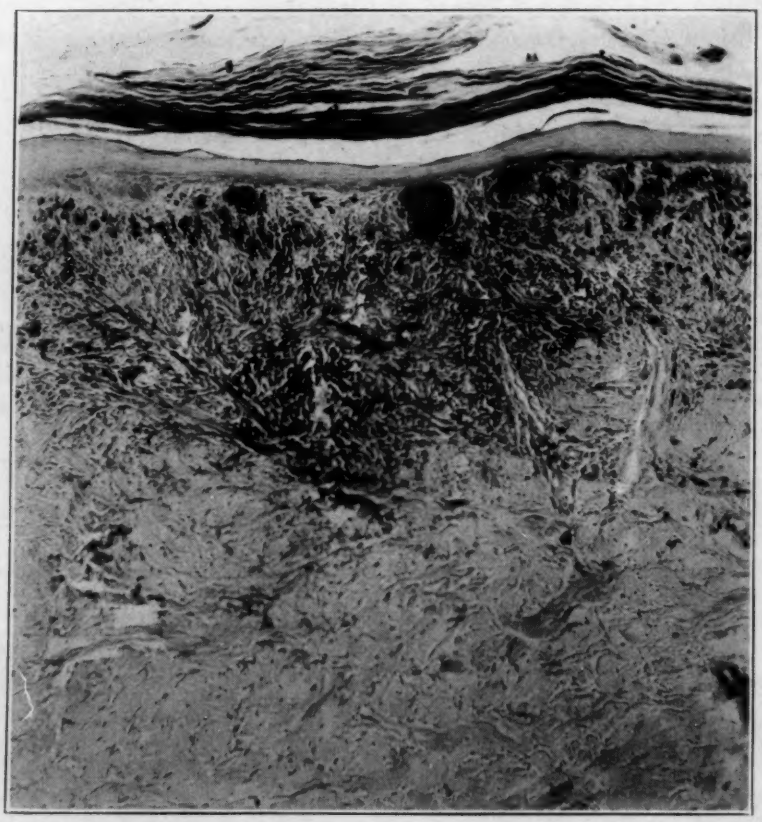


Fig. 2.—Photomicrograph showing deposits of iron in the upper portion of the corium and decided fibroblastic reaction about them (× 105).

with various remedies, among which were solution of boric acid, solution of sodium bicarbonate, alcohol and a solution of lead acetate of the approximate strength of a teaspoonful to a half-cup of water. After the use of the lead acetate solution she procured from her pharmacist some ferrous sulfate, made a solution of about a teaspoonful to a half-cup of water and applied it liberally to the eruption. A few days later many of the lesions turned brownish red.

The patient when examined presented many areas of dark red to brownish black pigmentation on the left side of the face and neck and on both forearms, more profuse on the flexor surfaces. The distribution of the lesions was in lines, angular

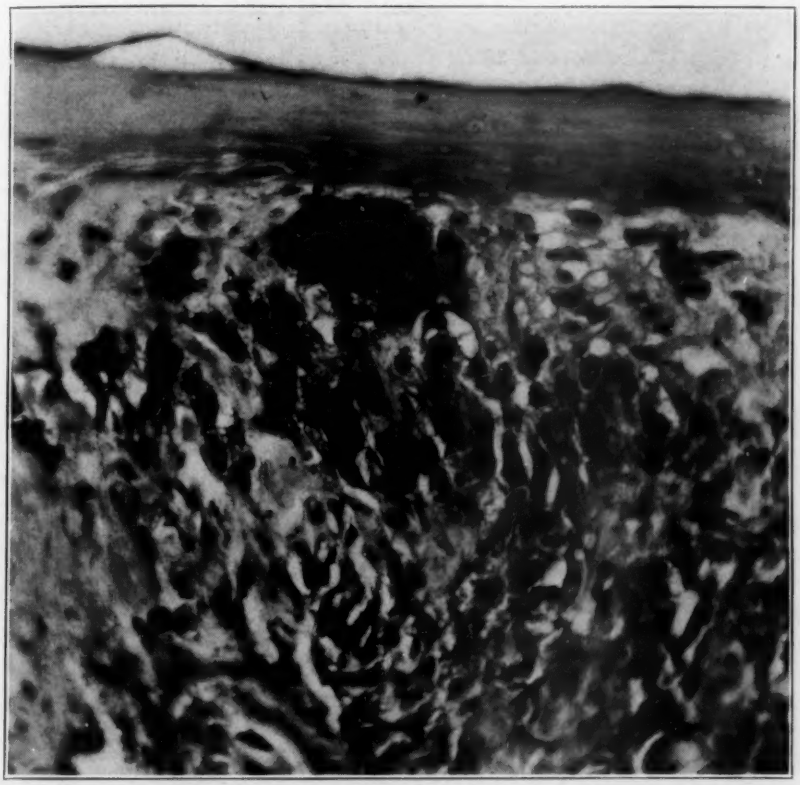


Fig. 3.—Photomicrograph showing macrophages containing iron granules and extracellular deposits of iron (× 380).

figures and irregular groups (fig. 1). Many of them resembled purpura when viewed from a slight distance. The lesions were level with the skin, did not fade on pressure and presented no infiltration appreciable to the touch. The individual lesions were from 1 to 5 mm. in size, mostly circular or oval and decidedly grouped.

When a section of a lesion was examined microscopically the epidermis was found to be somewhat atrophic and the horny layer somewhat hyperkeratotic (figs. 2 and 3). Throughout the upper third of the cutis, and particularly immediately adjacent to the basal layer of the epidermis, there was a heavy deposit of reddish

brown granules (in the section stained by the Turnbull blue method for the demonstration of iron pigment the granules were deep blue). The examination under higher power revealed that some of these deposits were free in the tissue spaces but that most of them were contained in large cells which were interpreted as chromatophores or macrophages. The deeper portions of the cutis were apparently free from these deposits in the sections with hematoxylin and eosin and in the sections stained with Turnbull blue. There was a decided fibroblastic reaction about these granular deposits.

The spectrographic analysis [15] showed a large amount of copper and a very large amount of iron present in the specimen. The calcium content was decidedly

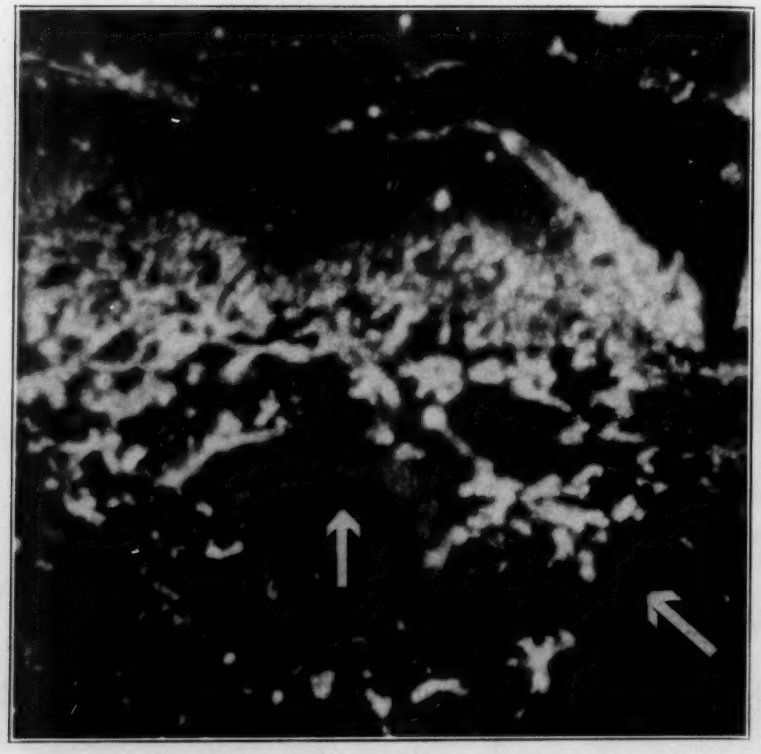


Fig. 4.—Dark field photomicrograph of microincinerated skin showing deposits of iron in the upper portion of the corium (indicated by arrows). The white ash of magnesium and calcium is well demonstrated in the epidermis (× 340).

low, while the magnesium content was high. No arsenic or gold was found. A faint trace of lead was present, although not enough to be considered abnormal in view of the history of the use of lead acetate applications. The silicon lines were not more intense than those found in normal skin. This spectrogram was

15. The significance of this article lies chiefly in the spectrographic and microincineration studies, which were done by Dr. Ross C. MacCardle, research associate to the Dermatologic Department of the Barnard Free Skin and Cancer Hospital.

not read microphotometrically or calculated, but from gross examination under the comparison ocular it was certain that the iron and copper contents of this piece of skin were far higher than those of any other specimen observed in our laboratories.

Microincineration of the section was done with the following results. The mineral residue of the epidermis appeared to be normal except in areas of previously active lesions, where the epidermal cells possessed huge amounts of the white ash of calcium and magnesium. Since the spectrogram indicated a large amount of magnesium and little calcium in the whole skin, it is reasonable to assume that this white ash was probably mostly magnesium, even though the white ash of magnesium is not distinguishable from that of calcium. In the cutis of the section subjected to microincineration there were many dense patches of iron residue deposited immediately beneath the epidermis, both where the epidermis appeared to be normal and in areas of actual lesions. By the use of the comparison ocular it could be seen that most of this iron was deposited in huge pigmented chromatophores or macrophages that were located in individual clumps beneath the basal layer of the epidermis. The pigment in these chromatophores was a greenish brown substance that did not resemble melanin (the dopa test was not applied). There was no pigment found in any of the epidermal cells. These iron-containing pigmented dermal cells were present beneath areas where epidermal vesicles had developed as well as under the adjacent normal epidermis.

Unfortunately, there is no reliable histochemical test for copper, and this element does not leave a characteristically colored ash on incineration. Iron, of course, leaves a brilliant brick red residue of iron oxide that is easily distinguishable.

Undoubtedly the lead found on spectrographic examination was deposited in the skin by the application of the lead acetate solution. The large amount of copper occurred as a contaminant of the ferrous sulfate. In the United States Dispensatory it is stated that commercial ferrous sulfate is far from being pure and besides containing some ferric sulfate it is usually contaminated with metallic and earthy salts, such as those of copper, zinc, aluminum and magnesium.

COMMENT

Sutton [5] stated the belief that iron, as the acetate, is deposited in the skin after the application of both lead acetate and solution of ferrous sulfate. The same thing happened in our case, but other reports in the literature make no specific mention of lead acetate having been used. However, it may have been used in many if not all of them, as lead acetate is commonly used by the laity in the treatment of rhus dermatitis. The patient reported on by Reyner [7] had applied a solution of ferrous sulfate and followed this with the application of buttermilk, and it is possible that the organic acids in the buttermilk may have precipitated the iron in the form of an organic salt similar to the acetate. However, it seems possible that cases may occur in which organic acids are not used in addition to the iron salt solutions.

In comparing our microscopic observations with those of Traub and Tenner,[4] we found that our sections did not show the changes in the prickle cells that they found nor was there any great dilatation of the blood vessels and edema of the upper part of the corium. These observers also found chromatophores about the blood vessels and between the collagen fibers of the upper part of the corium which showed blue granules when stained by Perl's method.

A few of the lesions on the arms of this patient were treated by infiltration with procaine hydrochloride and light curettement, and the result so far has been fairly good. We are, however, not attempting to treat the remaining lesions in the hope that they will disappear spontaneously in the course of time.

SUMMARY

A case is reported of disfiguring pigmentation of the skin following the use of a solution of ferrous sulfate in the treatment of dermatitis venenata due to rhus toxicodendron.

Iron and copper were deposited in the upper portion of the cutis, chiefly in chromatophores. This was proved by histochemical, spectrographic and microincineration methods.

As in 1 other case in the literature, lead acetate and ferrous sulfate had been used, but other cases of this condition have been reported in which the use of lead acetate had not been mentioned, and it is possible that such pigmentation may occur without the use of lead acetate.

Attention is called to the importance and significance of spectrographic and microincineration methods of investigation in cases of metallic pigmentation.

CONCLUSION

We believe that salts of iron should not be used in the treatment of dermatitis venenata in view of the facts that the disease is self limited, that relief may be obtained by other means and that the use of iron salts may be followed by very disfiguring and more or less permanent pigmentation of the skin.

FAMILIAL BENIGN CHRONIC BULLOUS DERMATOSIS

ANDREW G. FRANKS, M.D.
AND
EUGENE F. TRAUB, M.D.
NEW YORK

There have been reports in the past year or so of several cases of a dermatosis of the vesiculobullous type with features which would indicate that if it is not new, it is at least an unusual variation of a known cutaneous condition. Careful comparison of the histologic features and etiologic factors (or their consistent absence) seems to point to a single disease entity, although the disease has been variously diagnosed as keratosis follicularis (Darier) with vesiculation, familial benign chronic pemphigus and recurrent herpetiform dermatitis repens.

In view of the relative infrequency of occurrence and in order to establish additional diagnostic criteria, 2 cases are here reported in which the condition is similar to that in the aforementioned reports.

REPORT OF CASES

CASE 1.—P. S., an unmarried American bank clerk aged 35, was seen in April 1936. He sought treatment for a recurring eruption of the neck, first noticed by him in 1931. Since that time he had not been free from it for any prolonged period. Although the eruption appeared in any season, it usually occurred in the summer, when tight clothing and subsequent perspiration increased the discomfort. The patient found it exceedingly difficult to wear a collar; so at times he could not carry on his work. The only subjective symptom was pruritus, which varied in degree with the extent of the lesions. The lesions were located on the sides of the neck, sometimes unilaterally and sometimes bilaterally.

According to the patient, a small blister would appear, which soon ruptured and rapidly spread peripherally. After a few days the margins of the lesions became crusted. Many topical preparations had been used, some of which gave palliative relief. He found that wet dressings of solution of aluminum acetate N. F. or spirit of camphor kept the lesion dry and reduced the discomfort but did not alter its progress. The eruption disappeared spontaneously in a few days to a few weeks, only to reappear somewhere else on the neck. Sometimes the condition would persist for a number of months. The patient stated that his father and a brother had similar eruptions recurring over a number of years. They stated the belief that the attacks were kept to a minimum or were prevented by going without a shirt collar while working. There were not any signs of other cutaneous eruptions or any history of drug ingestion which might be relevant. Examination of the patient over the past four years has confirmed his description of previous occurrences. The lesions varied in number and location, usually beginning as

small vesicles, enlarging and oozing an amber-colored sticky fluid. After remaining moist for a few days, the area became erythematous and crusted, presenting the appearance of a ruptured bulla of impetigo. The crust could be removed with little effort. There was no pitting or scarring in the region of healed lesions.

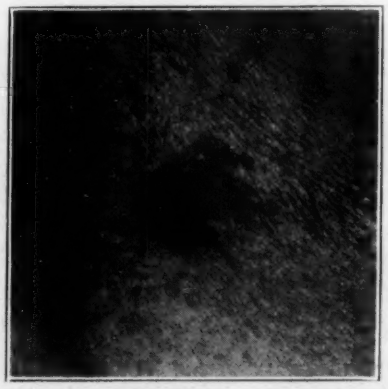


Fig. 1 (case 1).—Lesion on the neck of two days' duration.

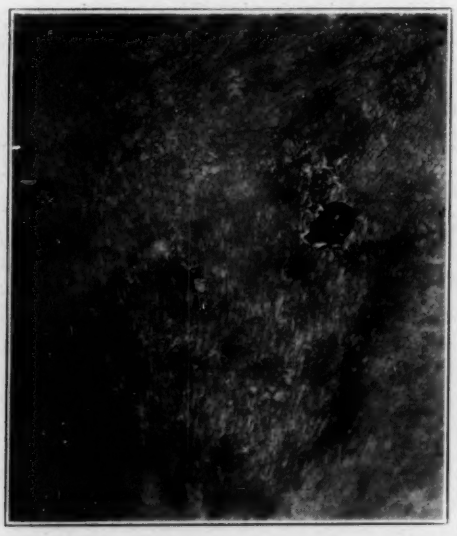


Fig. 2 (case 2).—Lesion on the neck of two weeks' duration (biopsy wound also shows).

nor was there any evidence of excoriation or adenopathy. The involved area varied in size from that of a dime to that of a palm. Nikolsky's sign was elicited.

The response to roentgen ray treatment was most interesting. After a fractional dose of 75 r the whole eruption disappeared and did not recur for a period of weeks to months. To date no other form of therapy has been given. The condition has been well controlled in the past four years, the patient having received a total of eight treatments totaling 600 r.

Laboratory data were unimportant. The Wassermann reaction of the blood was negative and the blood count normal. Bacteriologic and mycologic study of material from the lesion did not disclose any organisms.

CASE 2.[1]—J. A., a married Italian aged 29, employed as a motion picture operator, was seen recently for treatment of lesions similar to those in case 1. He related that for the previous six years he had lesions on the head, neck, axillas and groin, which appeared with frequent succession and simultaneously. These lesions sometimes healed spontaneously in three to eight weeks. He had received injections, but these did not alter the course of the disease. His mother and a sister had similar eruptions.

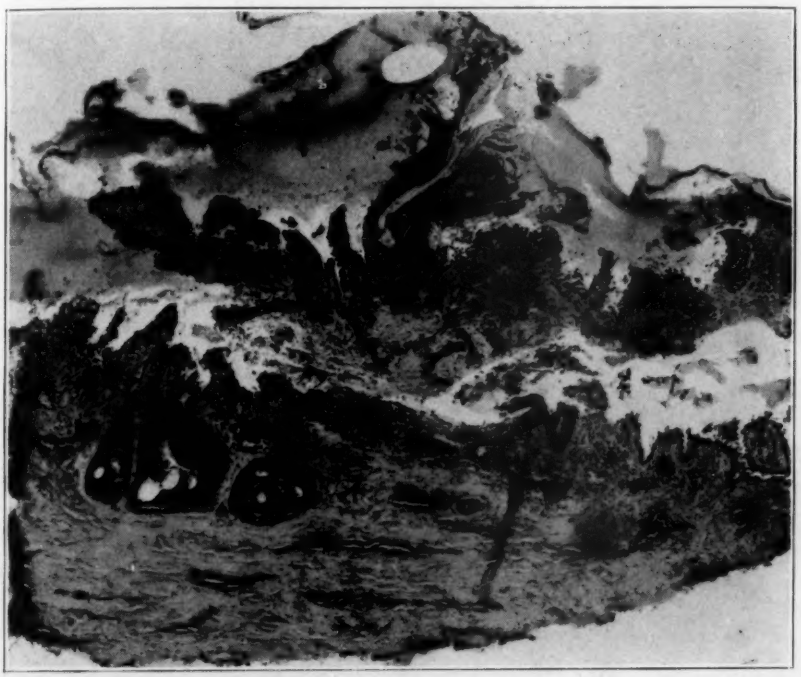


Fig. 3 (case 2).—Photomicrograph of a bullous lesion which splits the epidermis (× 60).

Examination showed crusted vesicles with amber-colored fluid on the occiput. There were several well defined bilateral lesions on the neck, about the size of a silver dollar, and a small lesion on the back of the neck. These lesions, as well as others in both armpits and in the right groin, had the same crusted vesicular appearance and an abundance of the typical sticky moisture. Laboratory examinations showed no abnormalities. Mycologic and bacteriologic studies gave normal results, and the Wassermann reaction of the blood was negative. Three superficial roentgen ray exposures (75 r) caused involution of the lesions.

1. This case was presented at a meeting of the New York Dermatological Society on Nov. 26, 1940 by Dr. Eugene F. Traub for Dr. Andrew Franks. It was agreed by those present that the condition in this case was the same clinically as that described by Hailey and Hailey.

HISTOLOGIC STUDIES [2]

Low Power.—The predominant pathologic changes were present in the epidermis. There was a large cavity, extending over the papillary bodies, which split the epidermis. The base of the bullous lesion was formed by basal cells; the roof was composed of epidermis which was

Fig. 4 (case 2).—Photomicrograph, showing changes in the cells of the epidermis (× 145).

in part thinned and in part slightly acanthotic. In the center of the cavity the roof had been torn in preparation of the specimen. The contents were composed of serum and at one point red blood cells (traumatic condition due to tearing of the surface of the cavity). In

2. Histologic examination was made by Drs. D. L. Satenstein and Wilbert Sachs.

the upper part of the cutis the vessels were only moderately dilated, and about them there was a moderate small round cell infiltration. Some of the vessels, especially at the edge of the section, were filled with blood cells. There was only a mild interstitial edema present.

High Power.—The basal cells comprising the palisade layer were of normal size, shape and staining characteristics. Above this zone the cells were rounded, and many were separated from one another. The nuclei were present in all the cells and were also round, well formed and well stained. The nucleoli were clearly visible. The cytoplasm of these cells showed normal staining characteristics. In this zone there were no prickle cells. The epidermis forming the roof of the cavity showed no pathologic change.

COMMENT

The literature contains reports of 10 cases of equivalent characteristics. Among these are found certain features which might lead one to conclude that there is some doubt as to whether or not all these cases are of the same disease entity. However, it is not the purpose here to show that every example or that any particular example of this unfamiliar dermatosis is the most typical. Questions without end may arise as to analysis of the histologic picture in several cases or even when specimens from a single lesion are considered. But two things are certain: There are similarities, and these similarities taken together may establish the basis for identification.

Reviewing briefly the outstanding equivalence, we noted that there is little doubt but that the disease is familial, that the cause is not established and that the course is benign and chronic. The lesions are vesicular and bullous; pruritus is usual, and temporary response to fractional roentgen therapy is generally acceded. Topical applications have proved only palliative and other forms of treatment either unsuccessful or inconclusive. The lesions occur most frequently on the neck and with diminishing frequency on the occiput, axillas, groin, back, abdomen and arms. One case was reported in which the conjunctiva and cornea were involved.

Careful and extensive search by Pels and Goodman,[3] by Hailey and Hailey [4] and by Ayres and Anderson [5] have failed to disclose a causative relation to drugs, organisms (bacterial or fungus) or organic conditions.

3. Pels, I. R., and Goodman, M. H.: Criteria for the Histologic Diagnosis of Keratosis Follicularis (Darier): Report of a Case with Vesiculation, Arch. Dermat. & Syph. **39**:438-455 (March) 1939.

4. Hailey, Howard, and Hailey, Hugh: Familial Benign Chronic Pemphigus, Arch. Dermat. & Syph. **39**:679-685 (April) 1939.

5. Ayres, S., Jr., and Anderson, N. P.: Recurrent Herpetiform Dermatitis Repens, Arch. Dermat. & Syph. **40**:402-413 (Sept.) 1939.

The eruption begins with small vesicles, which enlarge, forming flaccid bullae; as the lesions enlarge peripherally they usually rupture and an amber-colored crust appears. New lesions often occur while old ones are regressing. There is no scarring or pitting at the site of previous lesions; a pigmented area marks the site of recently healed lesions. Nikolsky's sign can be elicited.

Hailey and Hailey described 4 cases of "familial benign chronic pemphigus." Ayres and Anderson, although presumably reporting 5 similar cases, chose the name "recurrent herpetiform dermatitis repens." Goodman [6] subsequently wrote that the condition in a patient treated by him and Pels was similar to the entity described by Hailey and Hailey, contending, however, that the histologic evidence pointed to the conclusion that the disease in these instances was an example of Darier's disease of the vesicular type rather than a new entity. To this Dr. Hailey [7] recently replied, in a personal communication, that Goodman's disagreement as to the proper diagnosis probably arose from the fact that the condition in the 4 cases reported was not the same as that described by Pels and Goodman. We feel that there is some basis for this belief, although there is much similarity in all the reported cases to which we have referred.

Further study and comparison should lead to a designation regarding which there will be less uncertainty, so that any name would at present be expedient rather than final. Rein and Frank [8] suggested that the disease process be called "dyskeratosis vesiculosa hereditaria."

The histologic picture needs further investigation for any conclusive classification. Toward this end Sachs [9] has compiled, in a report as yet unpublished, the histologic changes and criteria for differential diagnosis of pemphigus, epidermolysis bullosa, Darier's disease, the Senear-Usher syndrome and similar related diseases. These will be studied closely and in detail.

Although not wishing to add further to the existing confusion of names, we feel that the condition herein reported should not refer to any of those already used or suggested. Pemphigus has already been attached as a title to too many disease entities, and since the cause of this variant—if it is a variant—is unknown, we believe it unwise for the present to adhere fully to the name first used by Hailey and Hailey.

---

6. Goodman, M. H.: Familial Benign Chronic Pemphigus, Correspondence, Arch. Dermat. & Syph. **40**:*272-273* (Aug.) 1939.

7. Hailey, H.: Personal communication to the authors, Aug. 23, 1940.

8. Discussion on Hailey and Hailey [4]; in Wise, F., and Sulzberger, M. B.: Year Book of Dermatology and Syphilology, Chicago, The Year Book Publishers, Inc., 1939, pp. 234-235.

9. Sachs, W.: Personal communication to the authors.

Until such time as the disease process is clarified and because of its descriptive significance we offer the name "familial benign chronic bullous dermatosis."

SUMMARY

Two cases of a dermatosis are reported in which there are several characteristics in common. In neither case was a causative factor discovered. Both patients had other members in their families who had had similar eruptions. The course of the disease was benign, no ill effects resulting from repeated attacks. Wet dressings and topical applications were only of temporary benefit, but superficial roentgen therapy caused rapid involution of the lesions. Histologic examination showed vesicle formation and changes in the cells of the epidermis which suggested dyskeratosis.

POSTRHAGADIC SCARS

ERNEST A. STRAKOSCH, M.D.
AND
LAWRENCE M. NELSON, M.D.
MINNEAPOLIS

The term rhagades, the plural of rhagas, is derived from the Greek word ῥαγας, meaning a tear, cleft or fissure in the skin or mucous membrane. In the contemporary literature, however, the term rhagades has been applied to designate scars on the lips, chin and cheeks and around the anus in persons with congenital syphilis. These lesions follow the healing of certain types of fissures in the involved areas. Histologically they are not true scars, although they appear to be so clinically. In this report the term rhagades is reserved for tears, clefts and fissures of the skin and mucous membrance and not for the healed lesions.

Although the pathologic changes in all syphilitic rhagades are identical, the discussion in this report is limited to lesions on the face.

Radiating scars around the mouth and rarely on the cheeks and chin are seen occasionally secondary to congenital syphilis; however, after a search of the English literature we were unable to find any report in which a differentiation was made between scars following syphilitic rhagades and those following nonsyphilitic fissures.

Since the publication of the original article on the subject by Friedinger, Mayr and von Zeissl,[1] in 1859, little has been added to the clinical description of the condition. Although their descriptions were excellent, they did not fully recognize the underlying pathologic changes. Subsequently Mayr[2] described the glistening rigidity of the facial skin in infants with congenital syphilis. He thought this was due to a syphilitic infiltration, having based his conclusion on clinical and not on histologic studies. Hochsinger[3] was the first who

From the Division of Dermatology and Syphilology, University of Minnesota, H. E. Michelson, M.D., Director, and the Department of Dermatology and Syphilology, Minneapolis General Hospital, S. E. Sweitzer, M.D., Chief.

1. Friedinger; Mayr, F., and von Zeissl, H.: Die Syphiliden im Kindes-Alter, Jahrb. f. Kinderh. **2**:1, 1859.

2. Mayr, F., and others: Ueber Syphilis hereditaria, Jahrb. f. Kinderh. **4**: 216, 1861.

3. Hochsinger, C.: Studien über die hereditäre Syphilis, Vienna, Franz Deuticke, 1898, pp. 170-196 and 229-242.

recognized and described the underlying pathologic changes of this condition, naming it diffuse hereditary syphilitic infiltration of the skin. He demonstrated that the infiltration begins as a diffuse process, in contrast to the localized infiltration found in a syphilitic papule.

In order to understand clearly the development of the postrhagadic scars, one must briefly review the clinical and histologic process prior to the scar formation. The earliest signs of the developing lesion usually appear as a diffuse infiltrate between the third and the seventh week of life. Jadassohn [4] stated that the areas involved, in order of frequency, are the lips, chin, cheeks and supraorbital regions. The color of the infiltrated skin varies with the age and location of the process. In the early stages it is bright red or coppery brown with a peculiar metallic sheen due to the abnormal tension of the epidermis. Old lesions assume a café-au-lait color.

The formation of rhagades is the result of the diffuse syphilitic infiltrative process. The number, formation, prominence and size of the rhagades are definitely dependent on the areas involved and on the amount of infiltration. Two factors, namely, the thinness of the epithelium and its mobility, predispose certain areas; therefore, the lower lip is more prone to the formation of rhagades than other areas of the face. The comparatively lesser mobility of the upper lip and of the skin of the face, in addition to the thicker epithelium of the latter, account for the relative infrequency of rhagades in these areas. The infiltrate causes tension and thinning of the epithelium and movement of the mouth produces further tension, with resultant rupture of the epithelium. These tears of the epithelium of the lip are always sagittal or perpendicular to the mucocutaneous border. In persons with extensive infiltration these rhagades may extend past the mucocutaneous border perpendicularly into the skin of the chin and upper lip. The epidermis of the cheeks in cases of severe lesions becomes stretched and thinned so that fissures form on movement of the muscles of facial expression in the same manner in which rhagades of the lip are formed. Rhagades do not always extend completely through the epidermis, and therefore they may heal without scaring. Occasionally secondary infection occurs, resulting in ulceration extending into the papillary layer of the skin and healing with true scar formation; however, in the majority of cases the healed rhagades are not true scars but apparent scars or areas of atrophy caused by a loss of elastic tissue in the cutis. The healed rhagades are linear and arranged radially around the mouth; later in life they may be the only remaining sign of congenital syphilis. Their occurrence is apparently not uncommon, but the stigmas may

4. Jadassohn, J.: Handbuch der Haut- und Geschlechtskrankheiten, Berlin, Julius Springer, 1927, vol. 11, p. 69.

be so slight that they are seen only on careful examination. Jeans and Cooke [5] found that of 707 congenitally syphilitic children over 2 years of age, 38, or 5.3 per cent, showed characteristic lesions about the mouth. Stokes [6] reported the stigmas in 6.5 per cent of 202 persons with congenital syphilis.

Hochsinger described three distinguishing characteristics of post-rhagadic scars in patients with congenital syphilis: (1) diminution of the red color of the lip and of the distinctiveness of the mucocutaneous border; (2) multiple, sagittally arranged deep, scarred furrows beginning at the mucocutaneous junction and extending back over the carmine portion of the lip (the favorite sites of these furrows are near the angles of the mouth on the lower lip and near the philtrum on the upper lip), and (3) extension radically of the previously described scars into the skin of the lip.

Hochsinger stated that the diagnosis of congenital syphilis can be made on the basis of circumoral scars only when all three of the preceding characteristics are present.

An interesting feature of this diffuse congenital syphilitic infiltration is its prevalence in areas of skin abundant in glandular elements. Hochsinger explained this phenomenon by the fact that spirochetes have a special affinity for all organs which are well developed in the fetus. In addition, Schneider [7] felt that a special reaction of the immature connective tissue and its hyperplasia could be contributory.

At the height of its development the syphilitic rhagas is covered with a necrotic crust. The underlying epithelium is loosened by serous imbibition, dilatation of the intracellular spaces and round cell infiltration. There are also in the epithelium variously sized hemorrhagic areas containing leukocytes and cellular debris. In the lower layers of the epidermis are many spirochetes, while in the cutis, where the infiltration is the heaviest, the spirochetes are comparatively few in number. Spirochetes are also found in the obliterated lumens of the blood and lymph vessels as well as in the ducts of the glands.

The apparent scar is histologically an atrophic area of elastic fibers rather than a true scar. In the involved areas Gans [8] reported that elastic fibers are destroyed leading to a depression of the epidermis which has lost its support. The papillary bodies are for the most part retained. The collagen is normal, and the epithelium in places is hypertrophic rather than atrophic.

---

5. Jeans, P. C., and Cooke, J. V.: Prepubescent Syphilis, New York, D. Appleton and Company, 1930, p. 143.

6. Stokes, J. H.: Modern Clinical Syphilology, ed. 2, Philadelphia, W. B. Saunders Company, 1934, p. 1239.

7. Schneider, P., cited by Gans.[8]

8. Gans, O.: Histologie der Hautkrankheiten, Berlin, Julius Springer, 1925, vol. 1, pp. 511-512.

REPORT OF CASES

CASE 1.—S. A., an 18 year old white school girl, came to the clinic of the Minneapolis General Hospital complaining of scars on her lips, chin and cheeks. Her mother stated that these scars were the result of eczema which the patient had in early infancy. When she was 7 years old an interstitial keratitis of the right eye developed, at which time the syphilis in both the mother and the patient was first discovered and treated.

Examination showed a diminution of the color of the lower lip as compared with that of the upper. The mucocutaneous junction of the lower lip was not clearly demarcated. The cheeks, chin and submaxillary regions were involved

Fig. 1 (case 1).—Postrhagadic syphilitic scars with retiform arrangement on the cheeks.

by scarlike lesions about 2 mm. wide. The lesions extended radially from the lip over the chin and left cheek. On the right cheek the lesions had a retiform arrangement enclosing normal skin. The lower lip had numerous sagittal furrows, many of which could be seen to be continuous with the previously mentioned lesions of the chin. With the exception of a high palate, all other observations, including laboratory tests, Wassermann tests and roentgen ray examination, were normal.

Two specimens of lesions in the submandibular region were taken for biopsy. A section of the first specimen (fig. 2), stained with hematoxylin and eosin, showed normal epidermis and rete pegs. The cutis appeared normal except for a slight increase in the density of the connective tissue in the papillary bodies. A

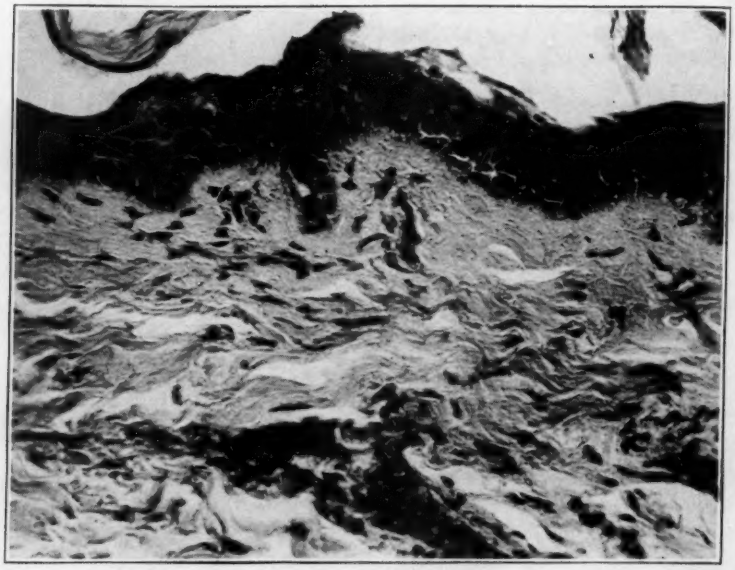


Fig. 2.—Photomicrograph showing increased density of the collagenous tissue in the papillary body.

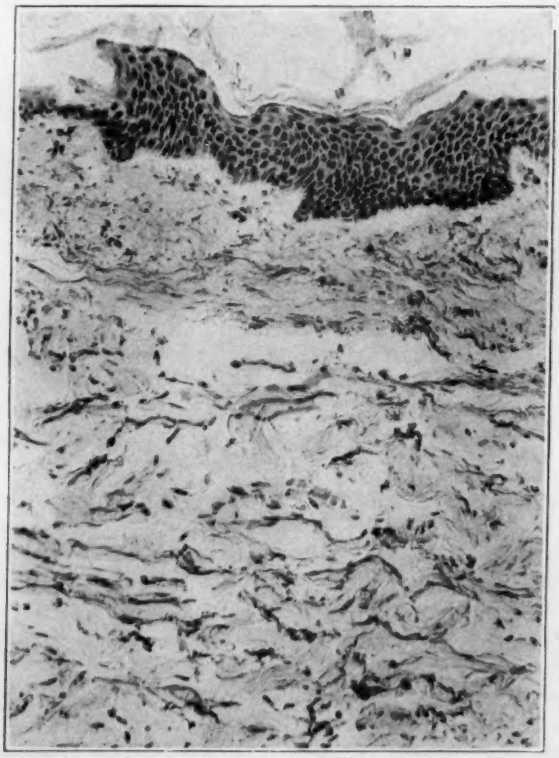


Fig. 3.—Photomicrograph showing absence of the elastic tissue in the papillary body.

section from the second biopsy specimen, stained with Weigert's elastic tissue stain (fig. 3), showed atrophy of the epidermis in the area of the lesion. Otherwise the epidermis was normal. The elastic fibers of the papillary bodies and of the papillary portion of the cutis were absent. The elastic fibers in the reticular part of the cutis were present but apparently diminished in amount. Glands were absent in both sections.

Fig. 4 (case 2).—Postrhagadic scars arranged as deep radiating sagittal furrows on the lip and chin.

Fig. 5 (case 3).—Postrhagadic syphilitic scars in the form of deep radiating sagittal furrows of the lips.

Case 2.—Mrs. H. H., a 32 year old white woman, had a condition diagnosed as congenital syphilis and was treated for it immediately after birth. At the time the patient had a diffuse crusted syphilitic infiltration with many rhagades involving the lips and chin.

Examination at the time of writing showed diminution in the intensity of color of the carmine portion of the lips. The mucocutaneous border was indistinct in

places. Numerous deep sagittal furrows involved both lips and extended radially into linear, scarlike lesions over the chin.

CASE 3.—D. B., a 9 year old white school boy, has had scars on both lips since infancy. His history, as obtained from his physician, was that he was born of a syphilitic mother who had received intensive antisyphilitic treatment for four weeks prior to the birth of the patient. At birth both lips of the patient were involved by diffusely infiltrated rhagades. Antisyphilitic treatment was immediately given.

Examination at the time of writing showed a diminution of the intensity of the color in the carmine portion of the lips. The mucocutaneous border appeared irregular and indistinct. Both lips had many deep furrows which extended radially into the linear scar on the chin and skin of the upper lip. Scarlike lesions also radiated from the angles of the mouth.

CASE 4.—L. B., a 24 year old white woman, stated that she had had scars around her mouth for as long as she could remember. Her mother had told

Fig. 6 (case 4).—Nonsyphilitic scars radiating from the angles of the mouth.

her that the scars had developed following bronchitis and eczema at the age of 18 months.

Examination revealed several superficial scars, 2 mm. in width, radiating from the angles of the mouth. The color of the lips was normal, and the mucocutaneous borders were distinct. There were no deep furrows in the carmine portion of the lip. A history of syphilis could not be elicited. Serologic tests for syphilis gave negative results. Physical examination otherwise revealed no abnormalities.

COMMENT

The first 3 patients had postrhagadic scars of congenital syphilis. The onset at birth or shortly thereafter and the clinical manifestation of a diffuse infiltration were noteworthy. The diminution of the normal color of the vermilion portion of the lip and partial obliteration of the mucocutaneous border were present in all 3. The furrows of the lip were sagittal to the vermilion border and continuous with linear scar-

like lesions on the skin of the chin and cheek. In case 1 the process on one cheek assumed a retiform arrangement. The linear furrows of the lips and scars of the skin were parallel. The configuration of the lesions was apparently dependent on the underlying muscles and was always perpendicular to them. This phenomenon also explains the retiform arrangement on the cheek in case 1, in which the muscles pulled in two principal directions at approximately right angles to each other.

The histologic sections showed a dipping and atrophy of the epidermis. The connective tissue of the cutis showed slightly increased density, and the elastic tissue was greatly diminished and in some places entirely absent. This observation accounts for the apparent scar, which in reality is an area of atrophy following a diffuse syphilitic infiltration, in addition to tears caused by the stretching of a thin infiltrated epidermis. In case 4 the lesions were present in a nonsyphilitic patient. The color of the lips was normal, and the mucocutaneous borders were distinct. The scars were present at the angles of the mouth but did not involve the lips. The direction of these scars is downward and outward, in contrast to the course of furrows caused by a syphilitic papule, which extend upward and outward from the angle of the mouth.

SUMMARY AND CONCLUSIONS

Three cases of postrhagadic scars of congenital syphilis and 1 case of nonsyphilitic postrhagadic scars are reported.

The following conclusions may be drawn:

1. Postrhagadic scars of congenital syphilis are distinguished by diminution in the color of the lip, by the partial loss of the mucocutaneous border and by the presence of linear furrows of the lip which extend into radial scarlike lesions of the surrounding skin.

2. The lesions, although they appear scarlike, are in reality atrophy of the elastic tissue and not true scars; they belong in the group of secondary atrophic conditions of the skin.

FIXED ERUPTIONS FROM VARIOUS DRUGS AND OTHER AGENTS

POLYVALENT SPECIFIC SENSITIVITY

E. WILLIAM ABRAMOWITZ, M.D.
NEW YORK

The term fixed was introduced by Louis Brocq [1] in 1894 to denote an unusual form of eruption that was produced by the ingestion of antipyrine. The chief characteristic of this eruption was that it recurred in the primarily affected area each time antipyrine was taken. Such lesions appeared usually as erythematous, pigmentary or erythematous vesiculobullous patches sometimes involving the mucosal orifices. The term fixed has been extended since then to various types of eruptions, whether urticarial, erythematous or eczematous, to conjunctival reactions and to motor and sensory disturbances and swellings (extracutaneous effects) that reappear as a result of the use of a drug or other agent, provided the exact site of the parent manifestation flared up each time.[2] In this sense recurrent herpes, bromodermas, iododermas and the discoid type of lupus erythematosus may also be included in this category, provided a recurrence develops in the same area.

The word fixed, contrary to its general meaning, when applied to a drug eruption does not indicate that such lesions are permanent or lasting, because the eruption is not expected to reappear if the cause is eliminated. There are no permanent sequelae except those that may develop as a result of secondary and unrelated causes. Usage has established the designation fixed for such manifestations, even though they may never repeat themselves, because the reaction site is fixed and is observed to appear in the previously affected area or areas should a recurrence develop.

The histologic features of the fixed drug eruptions conform to those seen in the banal dermatoses, be they urticarial, erythematous or eczematous in appearance. The subpapillary layer in eruptions in which pigmentation develops is apt to show a varying number of cells contain-

From the Skin and Cancer Unit of the New York Post-Graduate Medical School and Hospital.

1. Brocq, L.: Éruption érythémato-pigmentée fixe due à l'antipyrine, Ann. de dermat. et syph. **5**:308, 1894.

2. Abramowitz, E. W., and Noun, M. H.: Fixed Drug Eruptions, Arch. Dermat. & Syph. **35**:875 (May) 1937.

ing melanin. Mibelli,[3] from a study of a fixed erythema from antiyprine that had undergone regression, stated the belief that the perivascular infiltration and the pigmentary cells still present accounted for the tendency to flare up in situ. According to Simon [4] and Jausion,[5] these residua assume an imitative function. In other words, the area formerly affected is so conditioned that it imitates its response to a stimulus it had previously encountered.

Fixed eruptions are no longer believed to appear from the use of only a few drugs. The following drugs have been reported as having produced fixed lesions:

Acetanilid	Eucalyptus, oil of
Acetylsalicylic acid	Iodides
Acriflavine	Ipomea
Aminopyrine	Isacen
Antimony and potassium tartrate	Magnesium hydroxide (magnesia magma)
Antipyrine	Mercury
Arsenicals (acetylarsan, arsphenamines, mapharsen, tryparsamide)	Phenolphthalein
Barbiturates	Quinine
Bismuth salts	Salicyiates
Cinchophen	Sulfanilamide and its derivatives

Acetanilid, oil of eucalyptus, magnesium hydroxide and sulfanilamide represent additions to those published in 1937.[2] Most of the drugs responsible are of the synthetic organic variety; a few are simple inorganic chemicals (bismuth hydroxide, iodides, magnesium hydroxide and mild mercurous chloride). As the latter do not contain a benzene ring, it is a question whether any significance of an etiologic nature may be attached to those compounds which have such a nucleus as part of their structure. There is no apparent relation between most of these drugs that can furnish a clue for the cause of such lesions.

Besides the large number of chemical drugs enumerated, there are reports that vaccines, alcoholic liquors,[6] karaya gum,[7] and certain foods

3. Mibelli, V.: Su gli eritemi fissi da antipyrina, Gior. ital. d. mal. ven. **32**: 575, 1897.

4. Simon, C.: Troubles cutanées dans les névroses, in Darier, J., and others: Nouvelle pratique dermatologique, Paris, Masson & Cie, 1936, vol. 5, p. 841.

5. Jausion, in discussion on Gougerot, H.; Degos, R., and Varay: Psoriasis invisible. Resorption de l'éosin par une zone de peau, cliniquement et histologiquement normale, atteinte de psoriasis dix-huit mois auparavant, Bull. Soc. franç. de dermat. et syph. **45**:31 (Jan.) 1938.

6. Naegeli, O.: Ueber fixe Arzneiexantheme, Klin. Wchnschr. **6**:25 (Jan. 1) 1927.

7. Bowen, R.: Karaya Gum as a Cause of Urticaria, Arch. Dermat. & Syph. **39**:506 (March) 1939.

(lentils [8] and tomatoes [9]) have also produced a fixed type of eruption. Other more complex factors, such as physical exertion and psychic stress,[10] autotoxic substances (metabolites [11]) and menstrual disturbances,[12] have on occasions caused similar effects. The following reports indicate some unusual sequences in persons subject to fixed eruptions. In Naegeli's patient at first a fixed eruption developed from antipyrine; then it flared up after a psychic upset and finally after an inhalation of oil of eucalyptus.[13] Ehrmann [14] reported the case of a colleague with a fixed eruption of the genitals from antipyrine. The eruption sometimes failed to reappear after the use of antipyrine, while at other times it flared up without any medication. Wise [15] observed a patient with an eruption from phenolphthalein that reappeared from the use of a barbiturate. Chargin [16] observed a patient with a fixed eruption from arsphenamine that flared up after he was given phenolphthalein. Another reacted similarly to antipyrine, and still another to a bismuth compound. In 1 instance the fixed lesions from arsphenamine flared up only after the taking of an arsenical, while new fixed lesions appeared after the use of phenolphthalein.[17] I have seen a patient with fixed lesions on the hands with a history that phenolphthalein, barbital or magnesia magma caused a flare-up of the lesions.[18] It has been known that a polyvalent specific sensitivity may be present in the same patient not only to various drugs but to other agents as well. The same phenomenon apparently may appear in the case of the fixed eruption. Allowance must be made for the many pitfalls in excluding medication and also for some nonspecific and other unknown factors that may play a part in the development of a fixed eruption.

---

8. Urbach, E.: Ueber fixe nutritiv-allergische Exantheme, Klin. Wchnschr. **15**:1208 (Aug. 22) 1936.

9. Cooke, R. A.: Personal communication to the author.

10. Wohlstein, E., and Schmidt, L.: Ueber ein fixes Erythem, Dermat. Wchnschr. **89**:1766 (Nov. 2) 1929.

11. Gougerot, H.: Dermatoses autoanaphylactiques: Contribution à l'étude des auto-anaphylaxies, J. méd. franç. **19**:160 (May) 1930.

12. Ehrmann, S.: Das Antipyrinexantheme, in Mracek, F.: Handbuch der Hautkrankheiten, ed. 4, Vienna, A. Hölder, 1902, vol. 1, p. 654.

13. Naegeli, cited by Kleeberg, L.: Toxicodermien, in Jadassohn, J.: Handbuch der Haut- und Geschlechtskrankheiten, Berlin, Julius Springer, 1933, vol. 4, pt. 2, p. 350.

14. Ehrmann,[12] p. 657.

15. Wise, F.: Personal communication to the author.

16. Chargin, L.: Fixed Eruption Due to Arsphenamine, Arch. Dermat. & Syph. **37**:144 (Jan.) 1938.

17. Chargin, L.: Fixed Eruption in a Patient Sensitive to Arsphenamine and Phenolphthalein in Different Areas, Arch. Dermat. & Syph. **38**:474 (Sept.) 1938.

18. Abramowitz, E. W., and Russo, J. J.: Fixed Eruption from Magnesium Hydroxide Polysensitivity, Arch. Dermat. & Syph. **41**:707 (April) 1940.

Two reports [19] indicate that antipyrine may be present in the fixed lesions (bullous) produced by antipyrine. Apolant [20] and others reproduced a recurrence of a fixed eruption by rubbing a quiescent patch with an antipyrine ointment. Whether a particular drug can be demonstrated in fixed eruptions from other drugs is yet to be determined. I have never been able to find phenolphthalein or its conjugate in an eruption from that drug. Sandler [21] reported recently that he demonstrated the presence of phenolphthalein in the normal skin of a patient with a fixed eruption from that drug by means of the conventional scratch test with tenth-normal sodium hydroxide solution. I performed these cutaneous tests in 1 case according to the technic of Sandler and found nothing indicating the presence of phenolphthalein. Sandler [22] informed me later that he could not confirm his findings in another case. Lowenfish [23] stated the belief that he detected phenolphthalein in the skin by a cataphoretic method in a case of an eruption on the hands from phenolphthalein. Lowenfish performed this test on 1 of my patients with a similar eruption, with negative results.

The surface application and the intracutaneous and subcutaneous injection of the exciting drug in fixed erythemas due to such drugs as phenolphthalein, barbiturates and arsphenamine, have yielded mostly negative results. When a fixed eruption is of the eczematous type it may be possible by means of the patch test to obtain a positive reaction with the particular drug responsible.[24]

Kenedy [25] claimed to have succeeded in transferring sensitivity to phenolphthalein to 2 normal human subjects by having them take phenolphthalein before they were given an intracutaneous injection of phenolphthalein-sensitized serum (Walzer method). I repeated this experiment, with negative results. Rosenthal [26] obtained positive endermic reactions to phenolphthalein in rabbits apparently sensitized to phenolphthalein by the previous injection of homologous and heter-

19. Tonnel and Raviart: Érythèmes brilleux dus à l'ingestion d'antipyrine; leur pathogénie, Echo méd. du Nord **1**:18, 1897. Mibelli, V.: Ueber die fixen Antipyrinerytheme, Monatsh. f. prakt. Dermat. **26**:333, 1898.

20. Apolant, H.: Zur Pathogenese der localisierten Antipyrinexantheme, Dermat. Ztschr. **6**:67, 1899.

21. Sandler, I. L.: Phenolphthalein Eruptions: Report of Three Cases, M. Ann. District of Columbia **8**:255 (Sept.) 1939.

22. Sandler, I. L.: Personal communication to the author.

23. Lowenfish, F. F.: Treatment of Chronic Dermatitis by a Cataphoretic Method, Arch. Dermat. & Syph. **37**:797 (May) 1938.

24. Bernstein, F.: Überempfindlichkeit gegen Phenolphthalein, Dermat. Ztschr. **62**:368 (Dec.) 1931.

25. Kenedy, D.: Sulla ipersensibilità alla fenolftaleina, Gior. ital. di dermat. e sif. **75**:965 (April) 1934.

26. Rosenthal, S. R.: The Conjugation of Haptens in Vivo, J. Immunol. **34**:25 (March) 1938.

ologous serum containing conjugated phenolphthalein. Jacobs [27] was able to sensitize guinea pigs to phthalic anhydride, one of the intermediates used in the preparation of phenolphthalein. Autotransplant experiments in man with fixed eruptions from antipyrine, arsphenamine, barbiturates and phenolphthalein show that the area of cutaneous hypersensitivity lies either in the epidermis or in the neurovascular structure of the cutis.[2] There is no further information on the presence of the Prausnitz-Küstner reagins or other antibodies in fixed eruptions from some of the other drugs or from the more complex agents previously mentioned in the list of those causing the fixed eruption.

It has been shown in the fixed eruption that such manifestations are not related to the nature of the agent and are not a part of its physiologic or toxic action. It appears in persons who have been exposed to the particular factor for varying periods without any ill effects and who then for some reason become specifically sensitized to the particular agent. It is difficult to rule out previous exposure in all cases in which the eruption appears presumably with the first dose. The period in which the specific sensitization develops may be determined from analogy with other types of eruptions due to a specific hypersensitivity and is probably about seven to ten days. Once so sensitized the fixed eruption appears thereafter within a few hours after the particular incitant is encountered. Comparatively small amounts of the specific substance, smaller than those necessary to produce pharmacologic or toxicologic action, may cause a recurrence of symptoms. Even after an absence of many years, renewed use of the drug is apt to cause symptoms, thus eliminating cumulative action. The fixed eruption, like many other drug eruptions, occurs only in certain apparently predisposed persons, while a majority remain unaffected in spite of a deliberately planned increase in dosage. In some cases desensitization may develop, while in others, as shown in reports herein presented, specific polyvalent sensitivity to various unrelated agents may develop.

Atopic manifestations and passive transfer to animals found in proved allergic infectious and noninfectious responses and observed in some other drug eruptions are conspicuously absent or uncommon in fixed eruptions. A fixed drug eruption has not been produced so far in man or animals. Nevertheless, there are many criteria that point to an allergic hypersensitivity as a basis for the development of the fixed eruption, even though atopic symptoms and specific antibodies cannot be demonstrated (with rare exception) in those with this type of eruption.

---

27. Jacobs, J. L.; Golden, T. S., and Kelley, J. J.: Immediate Reactions to Anhydrides of Wheal-and-Erythema Type, Proc. Soc. Exper. Biol. & Med. **43**:74 (Jan.) 1940.

If the allergic basis of the fixed eruption is accepted as correct, it is not difficult to understand why various factors, whether a complex protein or a simple chemical, are capable of producing the fixed eruption. Early in the history of fixed eruptions, they were first attributed solely to antipyrine, then almost entirely to phenolphthalein. Judging from the 68 cases of the condition due to arsenicals observed by Chargin and Leifer [28] in New York during the past five years, the arsenicals are the most common cause of the fixed eruption.

Fixed eruptions due to specific sensitizing agents other than drugs are being reported more and more as attention is being focused on such possibilities. They may be nonspecific in nature, the result of synergistic effects, or perhaps due to other unknown factors. As reports of fixed eruptions due to other agents than drugs are accumulating, it may be stated that fixed eruptions are produced not only by simple chemical allergens (drugs) but also by other allergenic substances.

SUMMARY AND CONCLUSIONS

Fixed eruptions have been reported from numerous synthetic organic compounds and a few simple inorganic chemicals.

It may be stated that fixed eruptions are produced not only by chemical (drug) allergens but by other allergenic factors as well (vaccines, alcoholic liquors, foods, karaya gum, autotoxins, menstrual disturbances, physical exertion and psychic stress).

Polysensitivity to more than one drug or agent may be present.

The term fixed has been extended to include urticarial, erythematous and eczematous eruptions, conjunctival reactions and motor and sensory disturbances and swellings (extracutaneous effects) that appear as a result of the use of a drug (or other agent) provided the exact site of the parent manifestation flares up each time.

Although the eruption is designated as fixed and implies a permanent or lasting effect, the eruption will not recur if the cause is eliminated.

It is difficult to demonstrate the presence of the drug in the fixed eruption that it produces.

All criteria point to an allergic hypersensitivity as a basis for the development of the fixed eruption in which atopic symptoms and specific antibodies cannot be demonstrated (with rare exception). They may be nonspecific, the result of synergistic effects, or perhaps due to other unknown factors in some instances.

853 Seventh Avenue.

28. Chargin, L., and Leifer, W.: Fixed Eruptions Produced by the Arsphenamines, J. Invest. Dermat. **3**:443 (Dec.) 1940.

NORWEGIAN SCABIES

S. E. SWEITZER, M.D.
AND
L. H. WINER, M.D.
MINNEAPOLIS

Recently we had the opportunity of examining and treating a patient with Norwegian scabies. This condition must be rare in America, as it has been reported here only three times (Hessler,[1] Ravogli[2] and Anderson and Stout[3]). In the many years at the Minneapolis General Hospital, where we have observed many thousand cases of scabies, the case to be reported is the first of this type that has come to our attention.

The first cases of this condition were reported by Danielssen and Boeck[4] in 1848. They considered the disease a form of leprosy which was endemic in Norway at that time. Hebra,[5] in 1851, on a visit to Oslo, Norway, observed a similar case and gave the condition the name "scabies norvegica Boeckii." He published a short paper on the subject in 1852.[6]

In all cases Norwegian scabies was characterized by heavy thick yellowish brown dry crusts, located over the dorsa of the fingers, the paronychial folds, the nail beds and even the nails. The elbows, sacrum and scalp were involved in like manner. On removal of the crusts, the skin underneath was found to be reddened and moist.

Becker and Obermayer,[7] like Hebra, stated the belief that the infecting organism is the Acarus scabiei and that, owing to neglect, the condi-

---

From the Department of Dermatology and Syphilology, University of Minnesota, Dr. H. E. Michelson, Director, and the Department of Dermatology and Syphilology, Minneapolis General Hospital, Dr. S. E. Sweitzer, Chief.

1. Hessler, R.: An Extreme Case of Parasitism, Science **21**:125 (March 3) 1893.

2. Ravogli, A.: Scabies Norwegica, Cincinnati Lancet-Clinic **41**:59-63, 1898.

3. Anderson, N. P., and Stout, M.: Norwegian Scabies, Arch. Dermat. & Syph. **42**:499-500 (Sept.) 1940.

4. Danielssen, D. C., and Boeck, F.: Traité de la spédalskhed ou éléphantiasis des Gres, Paris, J. B. Baillière, 1848, p. 232.

5. Hebra, F.: On Diseases of the Skin Including the Exanthemata, translated and edited by C. H. Fagge and P. H. Pyesmith, London, New Sydenham Society, 1868, vol. 2, pp. 213-216.

6. Hebra, F.: Ueber eine in Norwegen beobachteten neue Form der Krätze, Ztschr. d. k. k. Gesellsch. d. Aerzte zu Wien **1**:390-402, 1852.

7. Becker, S. W., and Obermayer, M. E.: Modern Dermatology and Syphilology, Philadelphia, J. B. Lippincott Company, 1940, p. 490.

tion progresses to crust formation and hyperkeratosis. Toomey [8] stated the belief that the infecting organism is a different Acarus than that ordinarily causing scabies. However, Boeck and Hebra were able to transfer the disease from patients with Norwegian scabies to normal persons, and ordinary scabies resulted.

The condition is not a form of pustular scabies, since these patients, having a lowered sensitivity, do not scratch. In the earlier cases the condition was found to have been associated with leprosy, whereas in the later cases reported it was found associated with feeblemindedness [9] and poor hygiene.[10]

Fig. 1.—A patient with "Norwegian scabies," showing excessive crusting and thickening of the skin of the hand and fingers.

REPORT OF A CASE

P. L., a white orphan boy aged 14, living in a boarding home, had scabies in 1938 and was treated with compound ointment of sulfur N. F. at the clinic of the Minneapolis General Hospital. He was requested to return to the clinic in

8. Toomey, N.: Scabies of Animal Origin, Urol. & Cutan. Rev. **26**:473-489 (Aug.) 1922; cited by Sutton, R. L., and Sutton, R. L., Jr.: Diseases of the Skin, ed. 10, St. Louis, C. V. Mosby Company, 1939, p. 1340.

9. de Amicis, T.: Un nouveau cas de gale norvégieune ou croûteuse, in Neisser, A., and Jacobi, E.: Ikonographia dermatologica, Berlin, Urban & Schwarzenberg, 1910, vol. 1, p. 1.

10. Gaté, J.; Bachmann (Mme.); Cuilleret, P., and Moreau, P.: Gale norvégienne avec épidémie hospitalière et villageoise, Bull. Soc. franç. de dermat. et syph. (Réunion dermat., Lyon) **45**:1378-1383 (July) 1938.

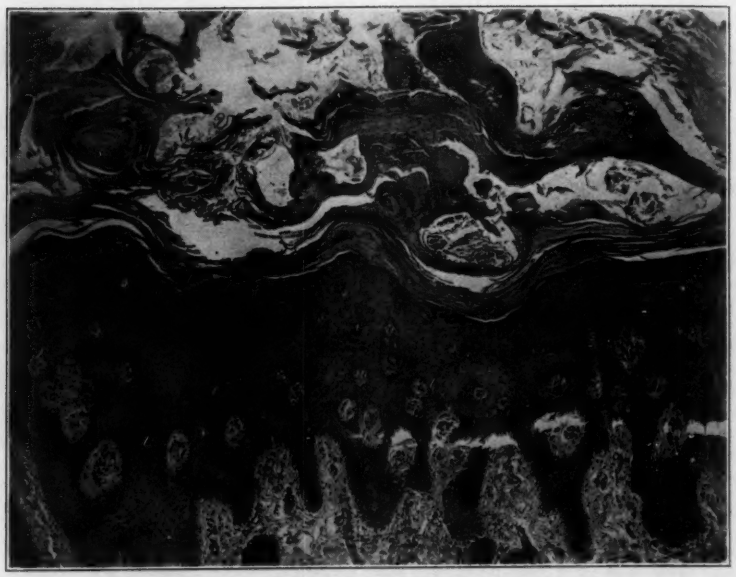


Fig. 2.—Section showing crust with multiple burrows.

Fig. 3.—Section showing ova of A. scabiei in a burrow.

one week, but he failed to keep his appointment. Not until June 9, 1940 was he seen again, and at this time he was hospitalized for treatment, which required twelve days.

Itching was first noticed three weeks before his admission. On examination there was decided hyperkeratosis of the palms, backs of the fingers, under the edges of the finger nails and around the nail folds. Lesions of a similar nature were present on the flexors of the wrists, on the penis and buttocks and around the umbilicus.

Acari scabiei were found in the scrapings from under the finger nails. Microscopic section of the lesion from the periungual region showed heavy crusts containing burrows arranged in tiers. The burrows were filled with many ova.

Consultation was requested from the neuropsychiatrist, who reported the result of an intelligence test as below 60 per cent (Terman's modification of the Simon Benet test)—that of a feebleminded child.

He was treated for nine days with compound ointment of sulfur N. F. and then examined. The lesions were still present on the finger tips. These areas were treated with the same ointment for three additional days, after which he was discharged as cured.

COMMENT

This patient was a feebleminded child and apparently did not complain of any severe itching. The condition was noticed by the caretaker only after clinical manifestations were severe. The three week history was given by the boarding home mother and not by the patient.

SUMMARY AND CONCLUSIONS

A case of Norwegian or crusted scabies is reported in a feebleminded child. It is our impression that this condition had existed since the first visit in 1938 (two years).

We conclude that Norwegian scabies is a hyperkeratotic form of scabies caused by A. scabiei and is never pustular and that it is the result of a long-continued neglected epidermal irritant, namely A. scabiei.

ASCORBIC ACID AND ARSPHENAMINE DERMATITIS

AN EXPERIMENTAL STUDY

FRANK M. McDONALD, M.D.
AKRON, OHIO
AND
HERBERT H. JOHNSON, M.D.
CLEVELAND

Although Frei,[1] in 1928, reported that he was able to produce cutaneous sensitivity to neoarsphenamine, there have been varied and conflicting reports on this phenomenon. The original work was confirmed in Germany by Mayer and Sulzberger,[2] but one of these workers was subsequently unable in New York to confirm his own previous work and also noted great variations in the same work in two different cities in this country.[3] Furthermore, it has been suggested that variations in the brand of neoarsphenamine might explain these conflicting reports.[4] In 1931 it was reported that a greater percentage of guinea pigs were sensitizable during the winter than during the summer months,[5] and the suggestion was offered that a dietary factor might play an important role.[3] In fact, it has been reported that the substitution of ascorbic acid

---

Dr. H. N. Cole and Dr. R. F. Parker gave valuable suggestions. Dr. Louis Pillemer gave advice and assistance.

Aided by a grant from the Therapeutic Research Committee, Council on Pharmacy and Chemistry of the American Medical Association.

From the Department of Dermatology and Syphilology, Western Reserve University. The facilities of the Institute of Pathology of Western Reserve University were used in this study.

1. Frei, W.: Ueber willkürliche Sensibilisierung gegen chemische definierte Substanzen, Klin. Wchnschr. **7**:539-542 (March 18); 1026-1031 (May 27) 1928.

2. Mayer, R. L., and Sulzberger, M. B.: Zur Frage der jahreszeitlichen Schwankungen der Krankheiten. Der Einfluss der Kost auf experimentelle Sensibilisierungen, Arch. f. Dermat. u. Syph. **163**:245-262, 1931.

3. Sulzberger, M. B., and Mayer, R. L.: Sensitizations: Regional, Seasonal, Dietary and Other Influences Accounting for Variations and Fluctuations, Arch. Dermat. & Syph. **24**:537-542 (Oct.) 1931.

4. (*a*) Tauber, E. B., in discussion on Schoch, A. G.: Arsphenamine Dermatitis, Arch. Dermat. & Syph. **30**:673-675 (Nov.) 1934. (*b*) Cormia, F. D.: Experimental Arsphenamine Dermatitis, Canad. M. A. J. **34**:272-276 (March) 1936. (*c*) Sulzberger, M. B., and Simon, F. A.: Arsphenamine Hypersensitiveness in Guinea Pigs, J. Allergy **6**:39-55 (Nov.) 1934.

5. Footnote deleted.

for greens offered protection against sensitization to neoarsphenamine.[6] Since then contradictory reports have appeared, one investigator [7] finding that ascorbic acid offered protection and others [8] finding that it had no influence.

In view of these conflicting results it was thought advisable to attempt neoarsphenamine sensitization in guinea pigs that were receiving varying quantities of ascorbic acid, controlling the ascorbic acid intake by injecting the drug intramuscularly, and to estimate the degree of ascorbic acid saturation by determinations of the ascorbic acid content of the blood at critical points in the experiment. A modification of Tillman's method of determining the ascorbic acid content of the blood was used,[9] and the results were repeatedly found to be correct to $\pm$ 5 per cent on solutions of weighed amounts of crystalline ascorbic acid.

The animals were divided into four groups. The first group was fed a commercial rabbit chow.[10] This diet is normal in all respects except for a deficiency of ascorbic acid, and it eliminates the starvation factor. The second group was given the chow plus 0.7 mg. of ascorbic acid daily. The third group was given the chow plus 2 mg. of ascorbic acid per day. The fourth group was given the chow plus 10 mg. of ascorbic acid per day.

The ascorbic acid was administered by intramuscular injection. The sites for intradermal injection of neoarsphenamine were prepared by manual epilation. All doses of neoarsphenamine [11] were 0.1 cc. of a 0.15 per cent solution. The two doses of neoarsphenamine were given at twenty-eight to thirty-eight day intervals to allow ample time for the development of sensitivity. The site of the last intradermal injection was observed for four weeks to detect possible delayed reaction. However, since no delayed reactions were encountered, the tabulated results are limited to the first week after injection.

---

6. Sulzberger, M. B., and Oser, B. L.: Influence of Ascorbic Acid of Diet on Sensitization of Guinea Pigs to Neoarsphenamine, Proc. Soc. Exper. Biol. & Med. **32**:716-719 (Feb.) 1935.

7. Cormia, F. E.: Experimental Arsphenamine Dermatitis: Influence of Vitamin C in Production of Arsphenamine Sensitiveness, Canad. M. A. J. **36**:392-396 (April) 1937.

8. (*a*) Chapman, C. W., and Morrell, C. A.: Influence of Vitamin C on Development of Skin Sensitivity to Neoarsphenamine in Guinea Pig, Proc. Soc. Exper. Biol. & Med. **32**:813-815 (Feb.) 1935. (*b*) Cohen, M. B.: Vitamin C Deficiency: Sensitivity to Neoarsphenamine and Anaphylactic Shock, J. Allergy **10**:15-26 (Nov.) 1938.

9. Ecker, E. E., and Pillemer, L.: Vitamin C Requirements of the Guinea Pig, Proc. Soc. Exper. Biol. & Med. **44**:262-263 (May) 1940.

10. Purina rabbit chow, made by the Ralston Purina Company, St. Louis.

11. The same lot of neoarsphenamine was used throughout. A dose of 0.02 Gm. of this produced generalized erythema in a human subject known to have had a mild arsenical dermatitis six years previously.

Determinations of the ascorbic acid content of the blood were made three times in each guinea pig studied, on the day of each of the two intradermal injections of neoarsphenamine and after the reaction at the site of the second injection of neoarsphenamine had subsided.

The vitamin C was given intramuscularly in the form of ascorbic acid or a sodium salt of ascorbic acid. Injections were made daily, or double the daily dose was given every second day. No differences were observed as a result of these variations in technic.

The cutaneous reaction observed was interpreted and recorded as follows:

No reaction	0
Erythema, slight	±
Erythema, greater than 5 mm.	1
An indurated nodule less than 5 mm. in diameter	2
An indurated nodule more than 5 mm. in diameter	3
Central necrosis	4

Differences between a 2 plus and a 3 plus reaction and between a 3 plus and a 4 plus reaction were not great.

The first groups consisted of 6 guinea pigs fed chow without the addition of ascorbic acid. All showed frank clinical scurvy at the end of the three weeks' observation period, and only 1 survived cardiac puncture, to die of scurvy eight days later. Ascorbic acid levels for 2 animals were 0.2 mg. and 0.14 mg. per hundred cubic centimeters, respectively. No opportunity was offered for the study of intradermal reactions.

In table 1 the ascorbic acid levels and cutaneous reactions of guinea pigs receiving 0.7 mg. of ascorbic acid daily are given. Several animals on which incomplete studies were made because of death are included mainly to show ascorbic acid levels. The animals showed an average gain in weight of 60 Gm. and no clinical signs of scurvy. The average ascorbic acid levels in the blood for the three times it was determined were 0.33 mg., 0.35 mg. and 0.29 mg. per hundred cubic centimeters, respectively.

In no instance in this group was the first intradermal reaction reactivated by the second intradermal injection of neoarsphenamine, and in no instance was an extensive or generalized reaction produced. In the individual cutaneous lesions 3 of the 12 animals showed increased reaction to the second injection of neoarsphenamine intradermally, but this bore no relation to the ascorbic acid levels in the blood.

Table 2 shows the results when 2 mg. of ascorbic acid daily was given. The animals showed an average gain in weight of 67 Gm. The

average ascorbic acid levels in the blood for the three determinations were 0.44 mg., 0.51 mg. and 0.45 mg. per hundred cubic centimeters, respectively. In this group there was no instance in which the first

TABLE 1.—*Animals Receiving 0.7 Mg. of Ascorbic Acid Daily*

Animal	Ascorbic Acid in the Plasma, Mg. per 100 Cc.			Reaction to First Injection of Neoarsphenamine		Reaction to Second Injection of Neoarsphenamine	
	At Time of First Injection	At Time of Second Injection	After Second Reaction Subsided	1-2 Days	3-7 Days	1-2 Days	3-7 Days
7	0.36	0.44	0.28	±	2	2	4
8	0.18	0.50	0.21	±	1	4	4
10	0.23	0.36	0.26	0	0	4	4
22	0.24	0.42	0.27	3	3	3	3
23	0.38	0.36	0.30	2	3	3	3
24	0.40	0.24	0.36	3	3	3	3
26	0.40	0.24	0.44	3	2	3	2
29	0.35	0.27	0.22	2	3	3	2
30	0.37	0.36	0.38	3	3	3	3
33	0.34	0.42	0.22	3	3	4	4
35	0.32	0.32	....	3	3	3	3
11	0.35	....	....	Died			
25	0.28	....	....	3	3	Died	
27	0.22	0.32	....	3	3	Died	
32	0.42	....	....	Died			
34	0.38	0.32	....	3	3	4	4
Average	0.33	0.35	0.29				
Median	0.35	0.36	0.27				

TABLE 2.—*Animals Receiving 2 Mg. of Ascorbic Acid Daily*

Animal	Ascorbic Acid in the Plasma, Mg. per 100 Cc.			Reaction to First Injection of Neoarsphenamine		Reaction to Second Injection of Neoarsphenamine	
	At Time of First Injection	At Time of Second Injection	After Second Reaction Subsided	1-2 Days	3-7 Days	1-2 Days	3-7 Days
12	0.72	0.49	0.44	±	±	3	2
14	0.44	0.62	0.47	0	0	2	4
15	0.47	0.68	0.41	0	±	3	2
36	0.46	0.34	0.40	2	4	3	3
37	0.40	0.58	0.48	2	2	3	3
39	0.34	0.48	....	2	3	3	3
40	0.38	0.57	0.47	2	2	3	3
41	0.42	0.48	0.45	3	4	3	3
43	0.46	0.52	0.49	3	3	3	3
44	0.50	0.66	....	±	2	3	3
45	0.32	0.40	....	3	3	3	3
47	0.42	0.40	0.41	3	3	3	3
48	0.36	0.56	....	3	4	3	3
50	0.44	0.48	....	3	2	3	3
49	0.48	0.44	....	3	3	3	Died
51	0.45	....	....	3	3	Died	
40	0.54	....	....				
38	0.34	....	....				
13	0.46	....	....				
16	0.45	....	....				
Average	0.44	0.51	0.45				
Median	0.44	0.49	0.45				

injection was reactivated by the second injection, and no extensive reactions were encountered. Six of 14 animals showed increased reaction to the second injection of neoarsphenamine intradermally, and this again bore no relation to the ascorbic acid levels in the blood.

Table 3 shows the results when 10 mg. of ascorbic acid was given daily. The average gain in weight was 185 Gm., and the average values for ascorbic acid in the blood were 1.21 mg., 1.06 mg. and 1 mg. per hundred cubic centimeters, respectively. The first injection was in no instance reactivated by the second injection, and no extensive reactions were encountered. Five of the 10 animals showed increased reaction to the second injection of neoarsphenamine intradermally, but this bore no relation to the ascorbic acid levels in the blood.

TABLE 3.—*Animals Receiving 10 Mg. of Ascorbic Acid Daily*

	Ascorbic Acid in the Plasma, Mg. per 100 Cc.			Reaction to First Injection of Neoarsphenamine		Reaction to Second Injection of Neoarsphenamine	
Animal	At Time of First Injection	At Time of Second Injection	After Second Reaction Subsided	1-2 Days	3-7 Days	1-2 Days	3-7 Days
17	4.00	1.12	0.85	0	0	3	3
18	0.92	0.98	1.04	2	3	3	3
19	0.90	0.92	1.02	0	0	3	3
52	1.21	0.97	1.02	4	4	3	3
53	1.12	1.13	1.12	2	2	3	3
54	0.94	1.06	0.97	2	2	3	3
57	0.97	1.07	0.97	2	3	4	4
58	0.89	1.07	1.02	2	1	3	3
59	0.96	1.21	0.96	2	2	3	2
64	1.34	1.06	1.00	3	2	3	3
20	0.90	....	....	1	2		
60	1.01	1.12	....	3	2		
62	1.12	....	....	3	2		
63	0.97	....	....	3			
21	1.22	....	....	Died			
55	1.00	....	....	Died			
61	1.11	....	....	Died			
Average	1.21*	1.06	1.00				
Median	1.00	1.07	1.01				

* The average excluding no. 17 was 0.98 mg. per hundred cubic centimeters.

COMMENT

Ascorbic acid has been reported as offering protection against experimental sensitization to neoarsphenamine [12] and also as having no influence.[8b] Another investigator found that the sensitization was more decided in animals receiving the larger doses of ascorbic acid.[8a] The results of this study show little difference and much overlapping in ascorbic acid levels in the blood between the groups receiving 0.7 mg. and 2 mg. daily. It was in this range of dosage that the two diametrically opposed results have been reported.[13]

It is also noteworthy that Cohen,[8b] who found ascorbic acid of no influence, carefully controlled his experiments by histologic study of dental changes. He also found that neither 0.7 mg. nor 2 mg. was protective against changes in the teeth and 5 mg. was not 100 per cent protective. It was only in guinea pigs receiving 10 mg. daily that con-

12. Sulzberger and Oser.[6] Cormia.[7]
13. Cormia.[7] Chapman and Morrell.[8a]

stant dental protection was given, and this corresponds with our results using the ascorbic acid level in the blood as an index, as well as extensive investigations of the ascorbic acid levels in the blood by others.[9]

If one assumes that any observable increase in reaction to the second injection of neoarsphenamine intradermally is proof of sensitization, 25 per cent of the group receiving 0.7 mg. of ascorbic acid, 43 per cent of the group receiving 2 mg. and 50 per cent of the group receiving 10 mg. showed sensitization. However, if only the definitely increased reactions to the second injections are used, the figures are 25, 28 and 33 per cent respectively, which is scarcely a significant difference in groups of this size. In no case was there any demonstrable protection against this reaction with the larger doses of ascorbic acid or higher levels of ascorbic acid in the blood.

Although Landsteiner and Jacobs have conclusively demonstrated cutaneous sensitization of guinea pigs to various substitution compounds of benzene,[14] a review of the literature on attempts at intradermal sensitization to neoarsphenamine, shows many unsuccessful or equivocal results. Also most investigators have obtained reactions of varying degree to the first injection.[14a] In the present study 2 plus to 4 plus reactions on the first day after the initial injection were obtained in 81 per cent of the 43 guinea pigs. Examination of the tables reveals that while 14 of the 34 animals showed increased reaction to the second injection, only 9 animals showed a definite increase. It should also be pointed out that 4 of the animals showing no increased reaction to the second injection had 4 plus reactions (i. e., necrosis) from the first injection. In other words, about 26 per cent showed definite "sensitization" and 12 per cent showed necrosis without a sensitizing injection.

In view of these results one can scarcely escape concluding either (1) that varying degrees of sensitivity (0.15 mg. of neoarsphenamine in saline solution intradermally) occur regardless of previous exposure or (2) that the drug is a primary irritant in this dilution and that the degree of reaction varied with the depth of injection or the physiologic state of the animal, or both.

With other technics of demonstrating the sensitivity reaction, namely anaphyalctic (anaphylactoid?) shock[15] or generalized erythema,[1] after

14. Landsteiner, K., and Jacobs, J.: Studies on the Sensitization of Animals with Simple Chemical Compounds, J. Exper. Med. **61**:643-656 (May) 1935; **64**: 625 (Oct.) 1936.

14a. Mu, J. W.: Regional Variations in Skin Hypersensitiveness to Neoarsphenamine in Guinea Pigs and Rabbits, Proc. Soc. Exper. Biol. & Med. **29**:783-784 (April) 1932. Frei.[1] Mayer and Sulzberger.[2] Sulzberger and Mayer.[3] Cormia.[4b] Sulzberger and Simon.[4c] Chapman and Morrell.[8a] Cohen.[8b]

15. Lauf, R.: Untersuchungen über die Salvarsanüberempfindlichkeit des Meerschweinchens, Ztschr. f. Immunitätsforsch. u. exper. Therap. **86**:49-64 (Oct. 3) 1935.

the injection by the intravenous or intracardiac route, the results have been more consistent. Here too, however, the cutaneous reaction, i. e., the generalized erythema, must be interpreted with caution, since large doses were given in proportion to body weight, and when massive doses of neoarsphenamine are given to human beings 45 per cent show morbilliform or urticarial eruptions.[16]

SUMMARY

Guinea pigs on a scorbutogenic diet with parenteral injection of measured amounts of ascorbic acid showed the following blood ascorbic acid levels: (*a*) A scorbutogenic diet plus 0.7 mg. of ascorbic acid daily (39 determinations) resulted in an average ascorbic acid level in the blood of 0.33 mg. per hundred cubic centimeters and a median of 0.34 mg. (*b*) A scorbutogenic diet plus 2 mg. of ascorbic acid daily (44 determinations) resulted in an average ascorbic acid level in the blood of 0.47 mg. per hundred cubic centimeters and a median of 0.46 mg. (*c*) A scorbutogenic diet plus 10 mg. of ascorbic acid daily (38 determinations) resulted in an average ascorbic acid level in the blood of 1.11 mg. per hundred cubic centimeters and a median of 1.02 mg.

No relation could be found in guinea pigs between the quantity of ascorbic acid administered parenterally (or the blood ascorbic acid level in the blood) and the sensitivity to repeated intradermal injections of 0.15 per cent neoarsphenamine.

Critical examination of the varying severity of the first or sensitizing reactions, as compared with the varying severity of the second or "sensitivity" reactions, would scarcely justify the conclusion that definite and indisputable sensitization was produced in any instance.

16. Chargin, L.: Massive Arsenotherapy by the Intravenous Drip Method, Arch. Dermat. & Syph. **42**:248-252 (Aug.) 1940.

DERMATITIS OF HANDS CAUSED BY LIQUID PETROLATUM IN A PROPRIETARY HAIR TONIC

REPORT OF A CASE

HENRY D. NILES, M.D.
NEW YORK

Hair tonics frequently produce dermatitis of the scalp and face, but in a review of the literature I was unable to find any report of dermatitis of the hands from this cause. On account of this unusual localization and the lack of involvement of the more delicate skin of the scalp, the site of application, the following case is reported.

REPORT OF CASE

H. M., a white man aged 50, consulted me on March 18, 1940 because of a nonpruritic dry scaly eruption on his palms, thumbs and fingers of five months' duration. About one month before the onset of the eruption he had started to apply a proprietary hair tonic daily to his scalp. He had rubbed this in chiefly with his right thumb and index and middle finger, being careful to prevent its flowing down on his forehead or face, and these areas had never been affected. The eruption on his hands had been present constantly for five months, except for two weeks while he was away from home and did not use the hair tonic.

Examination revealed an ill defined superficially scaly patch in the center of each palm; induration, erythema, scaling and superficial fissures on the tips of the thumbs and fingers, and slight erythema, scaling and thickening of the skin on the sides and palmar surfaces of the fingers. The tips of the right thumb and index finger were most severely affected. There were no vesicles or pustules, and the clinical picture was that of a subacute or chronic dermatitis. The dorsa of the hands and the feet were not involved.

On March 21 a patch test with a few drops of the tonic was made on the flexor surface of his left forearm, and two days later there was an itchy large bulla at the site of the test. The patient was instructed to stop using the hair tonic and was given a mild antipruritic cream and two weekly treatments of 75 r of unfiltered roentgen rays. On April 12 the eruption had disappeared except for slight scaling on the tips of the thumbs and on the tip and inner side of the right index finger, but there was still faint erythema at the site of the patch test.

At one time the hair tonic contained "39A" alcohol (18 Gm. of cinchonidine sulfate to 1 gallon of isopropyl alcohol), and in cases of dermatitis of the scalp and face following its use the condition was usually considered or proved to be due to the quinine content. For this reason, on April 30, patch tests with a 2 per cent solution of quinine hydrochloride, isopropyl alcohol, "39A" alcohol and bay rum were applied. Contrary to expectation, they all gave negative results. Through the cooperation of the manufacturers, I then learned that recently the formula for their product had been changed and that it no longer contained either quinine or "39A" alcohol but that it contained an essence consisting of the

oils of bergamot, orange, lemon, Bulgarian rose, lavender, orange flower, petigrains, linalyl acetate and "no. 58," and also contained "40M" alcohol, which is denatured with 3 per cent brucine sulfate. On June 19 patch tests with the essence and the "40M" alcohol were made on the flexor surface of the right forearm. The essence produced so much burning and itching that the patient removed the patch after five hours. The skin in the area was then bright red and somewhat edematous, and forty-eight hours after application there was a sharply outlined round red dry patch (figure). There was a small faintly red patch at the upper border of the site of the application of "40M" alcohol,[1] but no reaction in the rest of this area. On removal of the patch containing the essence the patient stated that the fluid came in contact with the tips of some fingers of each hand and that since then they had been sore, itchy, red, scaly and fissured. On examination the con-

Upper part, erythematous reaction to a patch test with the essence in the hair tonic. Lower part, red, scaly, fissured dermatitis of the palmar surfaces and tips of the fingers of the left hand after contact with the essence in the hair tonic.

dition of the finger tips (figure) was the same, in a mild form, as that on his first visit. On July 9 patch tests with a 1 per cent alcoholic solution of each of the nine ingredients of the essence were applied to the flexor surfaces of the arms. Forty-eight hours later all of these gave negative results, except for a faint erythema at the site of the test with the "no. 58" solution. When the patient was next seen, on July 17, there was still some erythema in this area. He stated that the skin of his palms and finger tips continued to be thin, dry, scaly, red and easily irritated. At this time 75 r of unfiltered roentgen rays was applied to each palm. One week later the same dose was repeated to the palms and also to the tips of the thumbs and fingers. On this date a patch test with a 1:12 solution of "no. 58" in 30 per cent alcohol, which is the dilution present in the

1. The reaction was probably due to contamination with a drop of the essence, as a subsequent patch test with the alcohol gave a completely negative result.

hair tonic, was applied to the flexor surface of the right forearm. Because of severe burning, the patient removed this after twenty-four hours. Forty-eight hours after application there was a large bulla with a tender, red base at the site of this test.

On further correspondence with the manufacturers it was learned that the "no. 58" solution comprises 85 per cent of the essence, which is one-twelfth of the entire tonic, and is composed of an odorless, unperfumed, highly refined, light liquid petrolatum, consisting of equal parts of the aliphatic hydrocarbons dodecane and tridecane, and another substance, the identity of which they did not wish to reveal unless it was definitely proved to be the cause of the dermatitis. They accordingly sent me a sample of "no. 58" without this secret ingredient. A patch test with a 1:12 dilution of this solution in 30 per cent alcohol produced so much burning that the patient removed it after seven or eight hours. At this time the skin at the site of the test was very red, and forty-eight hours later it was still extremely red and scaly.

Four controls were tested with the same solution. In 1 allergic person, who previously had reacted to patch tests with several other substances, there was a moderately severe reaction, but in the other 3 the tests gave negative results. Because of this observation the solution was considered not to be a primary irritant.

On September 9 a patch test with a 60 per cent solution of kerosene in liquid petrolatum gave a negative result. This showed that, although the patient reacted so strongly to the highly refined liquid petrolatum in the hair tonic, he was not sensitive to a more crude oil. The manufacturers averred that the oil which they use is only the distillate from common "white oil" and that no chemicals are employed in its refining. From these observations it appears that some quality of highly refined liquid petrolatum, perhaps the higher percentage of saturated hydrocarbons, causes a reaction in this patient's skin which does not occur with the much less highly refined kerosene. It was desired to perform patch tests with undiluted "no. 58" solution, with a mixture of "no. 58" in liquid petrolatum and with plain liquid petrolatum to determine if different solvents would alter the reaction, but the patient refused to submit to further testing.

COMMENT

The interesting and unusual features in this case are:

(1) The fact that a dermatitis on the hands proved to be due to a hair tonic, (2) the absence of eruption on the site of application, the more tender skin of the scalp, (3) the severe reaction to a plain highly refined liquid petrolatum and (4) the lack of reaction to a cruder liquid petrolatum.

In addition to the strongly positive reaction to a patch test with the tonic, the cause of the dermatitis on the hands was further proved clinically by its appearance shortly after the patient first used the tonic and its disappearance after use of the tonic was stopped.

This case illustrates the fact that a dermatitis of the hands can be caused by a substance applied by the patient to some other part of his body even though this part is free from eruption.

114 East Fifty-Fourth Street.

FIXED ERUPTIONS

REPORT OF AN UNUSUAL CONDITION DUE TO SULFANILAMIDE

M. H. GOODMAN, M.D.
BALTIMORE
AND
ROBERT D. ARTHUR, M.D.
SPRINGFIELD, OHIO

The cutaneous reactions to sulfanilamide occurring early in the course of therapy have undoubtedly been frequently precipitated by sunlight. Sensitization has only rarely been proved in these morbilliform, scarlatiniform, maculopapular and urticarial erythemas, for in many cases after temporary withdrawal of the drug the eruption promptly subsided and did not recur on its resumption.

In the reported cases of severe reactions in the skin from sulfanilamide, such as bullous and purpuric exanthems and exfoliative dermatitis, it is more than likely, especially when small or moderate doses of the drug have been administered, that hypersensitiveness has developed. Evidence has already accumulated to show that sulfanilamide can specifically sensitize the skin and bring about an allergic state. In one case there was a positive reaction to a patch test [1] and in another a suggestive positive reaction to a scratch test [2] and in a number of cases a small dose produced a recurrence of the eruption.[3] Stephan Epstein [4] has shown experimentally that sulfanilamide can produce not only a photosensitivity but a photoallergic state in the skin.

The most striking proof of the skin-sensitizing power of sulfanilamide is offered by a case of fixed eruption reported by Loveman and

---

From the Department of Dermatology, Johns Hopkins University School of Medicine.

1. Salvin, M.: Hypersensitivity to Sulfanilamide, J. A. M. A. **109**:1038 (Sept. 25) 1937.

2. Goodman, M. H., and Levy, C. S.: The Development of a Cutaneous Eruption (Toxicodermatosis) During the Administration of Sulfanilamide: Report of Two Cases, J. A. M. A. **109**:1009 (Sept. 25) 1937.

3. (*a*) Frank, L. J.: Dermatitis from Sulfanilamide, J. A. M. A. **109**:1011 (Sept. 25) 1937. (*b*) Schonberg, I. L.: Purpuric and Scarlatiniform Eruption Following Sulfanilamide, ibid. **109**:1035 (Sept. 25) 1937.

4. Epstein, S.: (*a*) in discussion on Tedder, J. W.: Toxic Manifestations in the Skin Following Sulfanilamide Therapy, Arch. Dermat. & Syph. **39**:217 (Feb.) 1939; (*b*) Photoallergy and Primary Photosensitivity to Sulfanilamide, J. Invest. Dermat. **2**:43 (April) 1939.

Simon.[5] They were able to reproduce the eruption in the exact locations not only by giving sulfanilamide again after the lesions had cleared up but also by giving azosulfamide, a closely related compound (disodium 4-sulfamidophenyl-2′-azo-7′-acetylamino-1′-hydroxynaphthalene-3′,6′-disulfonate). To confirm the results of these authors and because treatment was carried out uneventfully with sulfapyridine, we considered it worth while to report the following case.

REPORT OF CASE

History.—W. A., a robust 18 year old, dark brown–skinned Negro with an acute gonorrheal urethritis, ingested under the direction of a physician 60 grains (4 Gm.) of sulfanilamide on the night of July 7, 1940. This dose was reduced gradually to 30 grains (2 Gm.) daily, which was maintained until some time in the third week of August, when the urethral discharge had stopped. At this time, because of an itching eruption on the skin, the administration of the drug was discontinued. During the following week the eruption almost subsided, but because there was a reappearance of the discharge, he ingested 20 grains (1.3 Gm.) of sulfanilamide on August 31. Fifteen minutes after he took this dose there was a mild pruritus of the areas of the fading eruption, and on the following morning there was a full-blown recrudescence of the original lesions with an increase in their size. There was no history of atopic diseases or of any medication for months prior to the onset of the urethritis.

Examination.—The largest lesion and the one first to appear was on the anterior surface of the upper part of the right thigh. It was a round, palm-sized macular area of uniformly deep violaceous red with a finely scalloped border. Although the color was not completely blanched out on pressure, the minimal infiltration and edema suggested a superficial involvement of the skin. The majority of the lesions, which were identical, although smaller, were scattered mainly over the right side of the body. There were but a few lesions on the left side of the chest and scattered over the back and the pubic area. In all there were twelve to fifteen such violaceous patches. In addition to these characteristic colored macular patches of fixed eruption, there were discrete smooth hivelike somewhat tapering dome-shaped papules, ranging in size from 0.5 to 1 cm. in diameter and in color from a bright pink to a purplish red, which blanched easily on pressure (fig. 1). Such papules were arranged in two or more roughly concentric rings encircling each of the large violaceous patches with zones of normal skin, about 0.5 cm. wide, intervening. The association of a typical lesion of fixed exanthem with concentric groups of papules, that is, a corymbose pattern, so far as our experience with this type of eruption is concerned, is unique. Groups of such discrete papules were independently situated in the region of the left hip, on the front and back of the neck and on the dorsum of each hand. There were no lesions in the mouth, but the lips were dry and edematous with a violaceous red coloration adjacent to the vermilion border.

Further Observations.—With the avoidance of sulfanilamide after the flare-up on August 31, the eruption began to disappear a second time. On September 7 the patient was referred to the urologic clinic for his relapsing urethritis, where sulfapyridine therapy was instituted in doses of 1 Gm. thrice daily. This drug

5. Loveman, A. B., and Simon, F. A.: Fixed Eruption and Stomatitis Due to Sulfanilamide, Arch. Dermat. & Syph. **40**:29 (July) 1939.

had no effect on the eruption, which continued to bleach out gradually. On September 10 the urethral discharge had ceased. In spite of the continued administration of sulfapyridine in the same daily doses, the cutaneous lesions had faded out by September 22, except for a dusky residual pigmentation in the "fixed" areas. Administration of this drug was then discontinued.

On September 9 the level of sulfapyridine in the blood was 2.9 mg. per hundred cubic centimeters and on September 18 it was 3 mg. Throughout this period the white blood cell count and the hemoglobin percentage were normally maintained. The Wassermann reaction of the blood was negative, and the urine, after allowance for the changes incidental to the urethral infection, was normal. The general physical examination revealed no abnormality.

Fig. 1.—Violaceous maculoerythematous patch of fixed eruption on the anterior surface of the right thigh. The outlying concentric urticariopapular elements are an unusual feature.

EXPERIMENTAL OBSERVATIONS

In their case of fixed eruption (including stomatitis) from sulfanilamide, Loveman and Simon reproduced the lesion with a corresponding dose of azosulfamide, but it was not as intense or extensive as when sulfanilamide was given. They concluded therefrom that the azosulfamide was better tolerated because it liberated less para-aminobenzenesulfonamide, the portion of the complex chemical formula to which apparently their patient was sensitive. Instead of azosulfamide our patient received a drug related to the sulfanilamide group but of simpler chemical structure than azosulfamide, namely sulfapyridine (2-[para-amidobenzenesulfonamido]-pyridine).

On September 25, when the "fixed" areas on the patient's skin were presenting only a fading dusky outline, the patient was given by mouth a test dose of 10 grains

(0.6 Gm.) of sulfanilamide to see if the eruption could be reproduced. Ten hours later, heralded by itching of the lips, an intense pruritus appeared in all of the previously involved areas of the skin. There was a recurrence of the lesions in the original sites, both of the large violaceous erythematomacular patches and of the surrounding small urticariopapular elements. All of the patches showed a moderate increase in diameter by a new erythematous halo which was more edematous than the center of the lesion. However, the patches and their surrounding rings of

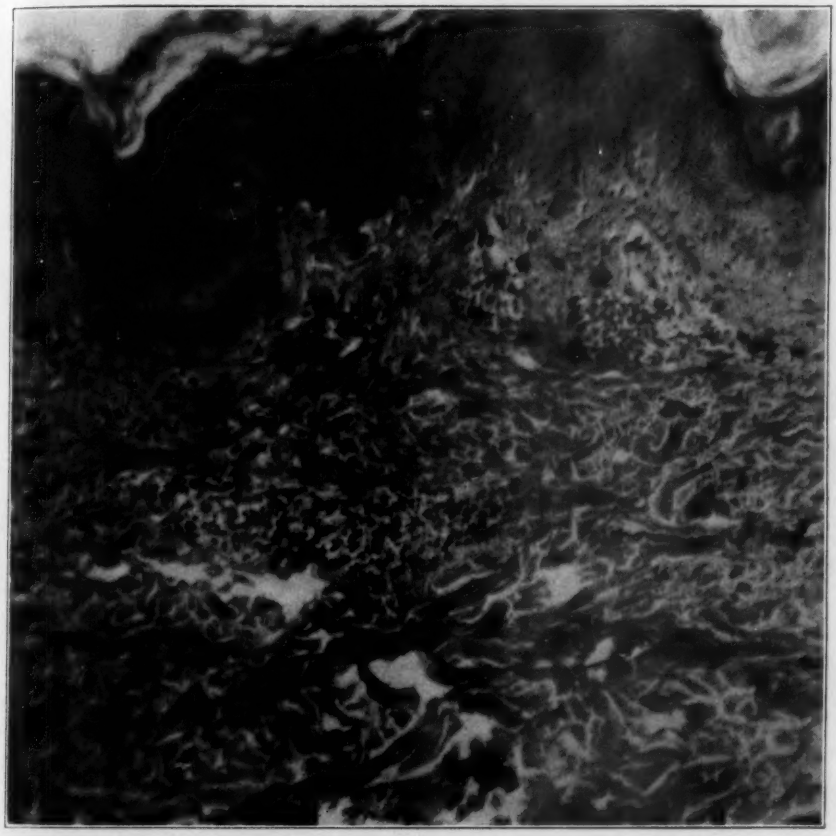


Fig. 2.—Photomicrograph, showing the inflammatory reaction located primarily in the papillary and subpapillary portions of the cutis. The absence of melanin in the epidermis and its concentration in large mononuclear cells about the narrowed blood vessels in the cutis are apparently characteristic features.

urticarial papules showed no deviation from their original relation and apparently appeared simultaneously. It was our impression that this episode was more severe but subsided more quickly than those caused by sulfanilamide unintentionally (during the third week of August and on August 31). The eruption began to fade for the third time forty-eight hours later.

Sulfapyridine administered in daily doses of 45 grains (3 Gm.) did not interfere with the healing of the eruption due to sulfanilamide. There was no recrudescence

of the eruption during the two weeks in which sulfapyridine was given. In view of the prompt curative effect on the gonorrheal urethritis in this case, it would seem that the tolerance to sulfapyridine in a patient intolerant to sulfanilamide may be of practical importance generally.

Since Loveman and Simon's patient was intolerant to both sulfanilamide and azosulfamide and our patient to sulfanilamide but not to sulfapyridine, it would appear, on examination of the formulas of the three compounds, that the allergic hypersensitivity to these drugs may, at least in some cases, be directed toward an ultimate chemical structure in which the amino (NH_2) radical remains unsplit in the sulfonamide (SO_2NH_2) group as the latter is bound to the aniline or paraaminobenzene nucleus.

Tests were performed on the patient's skin to determine whether it would give evidence by the usual criteria of the allergic hypersensitivity which existed. Separate areas of pigmentation on the right arm remaining after the lesions had resolved were used as the sites for the tests. A patch test with moistened sulfanilamide powder gave negative results after forty-eight hours. A scratch test with sulfanilamide powder also gave negative results. For the intradermal test an 0.8 per cent solution (the solvent being a one-sixth-molar solution of sodium lactate) of sulfanilamide was used. This injection gave no reaction immediately or after forty-eight hours. The passive transfer of reagins (Prausnitz-Küstner reaction) was attempted but was not successful.

Histologic Studies.—A biopsy segment from the border of a large "fixed" lesion showed in sections stained with hematoxylin and eosin a slight thickening of the horny layer but no changes in the stratum lucidum or stratum granulosum. The prickle cells showed clouding of the nucleus and cytoplasm, which resulted in a slight thickening of the rete. The cells of the basal layer were hydropic. No melanin pigment was to be seen in the epidermis. The inflammatory process in the cutis was strictly limited to the blood vessels and their immediate environs in the papillary and subpapillary layers. The blood vessels showed decided swelling of their walls with rounding out and constriction of the lumens. They were surrounded by a zone of edema in which there was an intense infiltrate composed chiefly of lymphocytes, interspersed, especially at the margin, by a great number of large mononuclear cells laden with deep brownish melanin pigment (fig. 2). These observations correspond well with those of histologic studies being made by one of us (M. H. G.) of fixed eruptions produced by some other drugs.

COMMENT

The site of hypersensitivity in the fixed eruption is as yet unknown. Some experiments[6] have shown that reaction will take place in an area of skin of fixed eruption which has been transplanted as a full thickness graft to an area from which an equivalent piece of normal unreactive skin has been excised. This would indicate that the sensi-

6. Naegeli, O.; de Quervain, F., and Stalder, W.: Nachweis der cellulärer Sitz der Allergie beim fixen Antipyrinexanthem, Klin. Wchnschr. **9**:924 (May 17) 1930.

tivity resides in the skin. Other experiments [7] suggest that the sensitivity is determined from below the skin by nerves or blood vessels because the transplanted skin of fixed eruption failed to react whereas the equivalent excised normal skin replacing it did. The occurrence in our case of the peculiar arrangement of the typical (fixed) lesion with outlying rings of papules appearing as a corymbiform unit has been of interest to us as possibly signifying that the hypersensitivity resides in the deeper position, perhaps nerves or blood vessels, at the site of the lesion. It is, of course, likely that the antigenic drug (sulfanilamide) would reach the outlying zones of papule formation by diffusion from the central "fixed" patch. However, the formation simultaneously of the various components of the corymbose unit could also be explained by the allergic phenomenon taking place at a deeper site, such as a nerve or blood vessel, which encompasses the entire unit in its zone of supply. If this presumption is true, then one might view the lesion of fixed eruption as only the expression in the skin of a local deeper hypersensitivity.

Two features of the microscopic picture in this case deserve special attention. These are the changes in the blood vessel walls, and, more particularly, the apparent tendency for complete absence of melanin in the basal cells and its accumulation in large mononuclear cells about the vessels of the subpapillary portion of the cutis. It seems to us that the peculiar violaceous red color of this type of eruption finds a reasonable explanation in these phenomena. We are inclined to believe that these features are characteristic, if not pathognomonic, of the fixed exanthem.

SUMMARY

A case is reported of fixed eruption with unusual features produced by sulfanilamide; the related compound sulfapyridine was nonprovocative.

What appear to be the characteristic histologic features of the usual lesion of this type of eruption are presented.

The question of the site of hypersensitivity is discussed in the light of the unusual clinical features in our case.

---

7. Wise, F., and Sulzberger, M. B.: Drug Eruptions: I. Fixed Phenolphthalein Eruptions, Arch. Dermat. & Syph. **27**:549 (April) 1933.

DERMATITIS FROM INDIRECT EXPOSURE TO FUR DYE

REPORT OF A CASE

HENRY D. NILES, M.D.
NEW YORK

M. P., a white housewife aged 32, born in the United States, was first seen at the Skin and Cancer Unit of the New York Post-Graduate Medical School and Hospital on March 9, 1940. On Nov. 22, 1939 circumscribed edematous vesicular patches, the shape of fingers, suddenly appeared on her neck, forearms and legs and the right side of her face. This eruption disappeared in a short time, although she later had similar lesions, which also involved the vulva but which soon completely disappeared. The third attack started on March 7 with sharply outlined red edematous vesicular patches, the exact shape and size of fingers, on each arm and an ill defined red vesicular dermatitis on her face, neck, breasts, legs and right labium majus. Her arms and breasts had never before been affected. In each attack there were lesions in the form of finger marks, and the eruption was very itchy. Since it first appeared she had used calamine ointment, calamine lotion, potassium permanganate baths and various salves, without relief.

There were no allergic diseases in the patient's family, and her skin had always been clear until January 1936, when she spent ten days in Kings County Hospital because of an itchy generalized weeping dermatitis. This was considered to be due to a dye, but it completely disappeared in two weeks with no treatment except application of a salve. Before the onset of her eruption in November 1939 she had worked for two and one-half years packing wooden boxes in a pencil factory, but she had not worked since then. She had been married for eleven years. Her husband had been a fur dyer for thirty-two months, but he had worked with aniline dyes for only the previous eight months. After work he cleansed his hands with a solution of potassium permanganate followed by a sodium bisulfite solution and a strong soap, and although he was unable to remove the dye completely, he had never had any itching or eruption. Although both of his palms and the palmar surfaces of his fingers and both thumbs were stained dark brown with the dye, there was no evidence of any dermatitis (fig. 1). Their 9 year old boy had no eruption.

The patient had a diffuse ill defined erythematopapulovesicular dermatitis on her face, neck and breasts, sharply outlined erythematous edematous vesicular patches, the exact shape and size of her husband's fingers, on the extensor surface of the upper part of each arm and similar but less sharply outlined patches, suggesting finger marks, on the right side of the neck, the inner side of each thigh and the right labium majus.

A mild soothing paste was prescribed, and one week later she was somewhat better. At this time she was given an antipruritic powdery emulsion, and a patch test with 2 per cent paraphenylenediamine in petrolatum was applied to the flexor

---

From the Skin and Cancer Unit of the New York Post-Graduate Medical School and Hospital.

surface of her left forearm. Forty-eight hours later there was an itchy erythematovesicular reaction at the site of the test (fig. 2). A similar patch test on her husband's arm gave completely negative results.

Fig. 1.—Hands of the patient's husband, with stain from dye still present after cleansing with chemicals and soap.

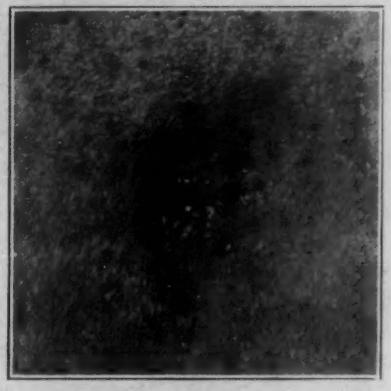


Fig. 2.—Erythematovesicular reaction to a patch test with paraphenylenediamine on the patient's forearm.

On April 11 she still had itching of the vulva and some dermatitis in the form of finger marks on the extensor surface of the right arm and the left forearm, but the definite finger prints on her arms and thighs had disappeared and she

was much better. Her husband had been wearing gloves while at work, and his hands were much less stained.

When next seen, on May 20, she had sharply outlined dull red patches of dermatitis, the shape of her husband's right hand and fingers, on the outer side of her left shoulder (fig. 3) which, she stated, had been present for three weeks. Fainter patches could still be seen on the extensor surface of her left forearm, but the rest of her skin was clear. The itching of the vulva continued, although there was no eruption in that area.

On June 6 she had a large bulla on the dorsum of her right wrist (fig. 4*A*) and a red wheal, the size of a palm, as well as an erythematous vesicular eruption, on the inner side of her left arm (fig. 4*B*). These had been present for only two days. Pigmented remains of former lesions were still visible on her left shoulder and forearm, and she continued to complain of pruritus vulvae, but there were only slight edema of the right labium majus and faint erythema in each groin. A patch test with fluid from the bulla on her right wrist applied to the flexor surface of her right forearm gave negative results in forty-eight hours. At this time it was learned that her husband while at work leaned against the edge of a table covered with dye. This caused the skin around his waist to be stained by the dye, although it produced no eruption or itching. He suggested that contact with the dye on his abdomen accounted for his wife's pruritus vulvae.

Fig. 3.—Patient's left shoulder, showing erythematous patches of dermatitis in the exact shape of the husband's right hand.

He, however, refused to change his work and was not careful about wearing gloves while working. Two days later the wheals on his wife's left arm were worse and there was a smaller one on the anterior fold of the left axilla. On June 18 her condition was much improved. She was last seen on October 22, at which time she had an ill defined red scaly dermatitis on her face, neck, chest and arms. There were a few roughly finger-shaped patches on the outer side of her right arm and forearm, two more definitely finger-shaped lesions on the inner side of her left arm near the axilla and faint remains of the former patches on her left shoulder. She stated that her husband no longer leaned against the dye-stained table and that the discoloration of the skin around his waist and her pruritus vulvae had disappeared. Recently 3 men who worked in the same place with her husband had had dermatitis of their hands, but he had not been affected. He had constantly worn gloves while working with the dye, but at times the dye came through and his hands were still stained.

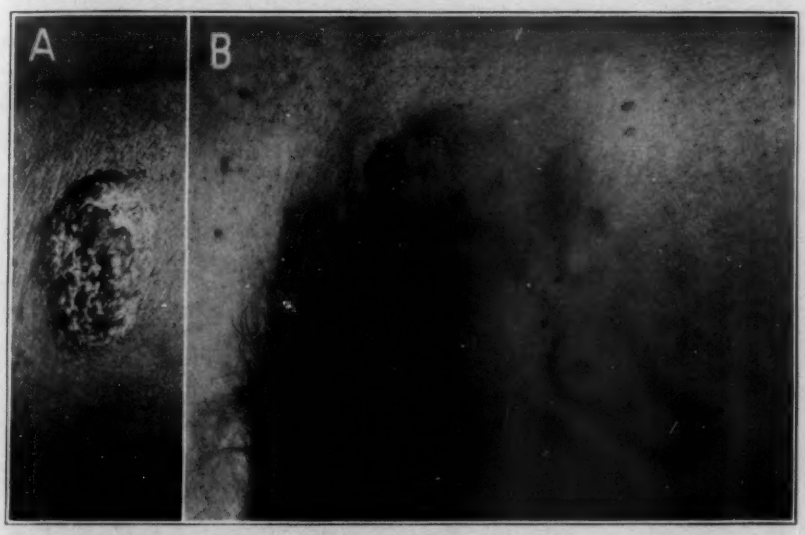


Fig. 4.—*A*, bulla on the dorsum of the patient's right wrist. *B*, erythemato-vesicular urticarial eruption, roughly in the shape of the husband's fingers, on the inner surface of patient's left arm.

Two weeks before the patient had worked for two days in a pencil factory, but she had been forced to stop work because of an eruption which had appeared on her face. This disappeared after she stopped working, but a similar rash appeared later while she was home. She has not replied to requests that she return to the clinic so that attempts to desensitize her to paraphenylenediamine have not been possible.

COMMENT

This case is reported because of the unusual finger-like shape of many of the patches, the frequent limitation of the dermatitis to these sharply defined areas and the patient's extreme sensitivity to paraphenylenediamine, as evidenced by the strongly positive reaction to the patch test and the production of dermatitis by the small amount

of dye remaining on her husband's hands after they had been thoroughly cleansed with strong chemicals and soap. The patient was unable to obtain these chemicals and the soap for patch tests, but in view of the strongly positive reaction to the patch test with paraphenylenediamine and the improvement in the patient's eruption whenever her husband protected his hands from exposure to the dye or carefully removed it, there seems to me to be no question of the cause of the dermatitis.

This case again illustrates the fact, in proof of which there have already been several reports, that a highly sensitive person may acquire a dermatitis from some substance with which he comes in only indirect contact through another person. This intermediary, if not sensitive to the substance, has no dermatitis. In this case the patient's husband gave no reaction to the patch test with paraphenylenediamine and had no dermatitis. This possibility of indirect exposure should be considered in cases of dermatitis in which the cause has not been determined.

114 East Fifty-Fourth Street.

Clinical Notes

DERMATITIS CAUSED BY LIPSTICK IN METALLIC CONTAINERS

J. C. Hathaway, M.D., Spokane, Wash.

Recently I have seen 2 patients with dermatitis due to the use of lipstick in metallic containers, both of whom were able to use lipstick in plastic containers. As far as I have been able to determine, similar instances have not been mentioned in the dermatologic literature.

The first patient, Mrs. M. K., a telephone operator, had consulted me five years previously for a contact dermatitis of the hands, which proved to be due to the handling of metal plugs used on the switchboard.

The second patient, Miss B. H., had consulted me two years previously for a contact dermatitis of the wrist, which proved to be due to a metal bracelet.

Both patients were given patch tests with lipstick taken from several metallic and plastic containers, and in both cases positive reactions were elicited with the lipstick from metallic containers and negative reactions with that from plastic containers.

The fact that there had been previous sensitization to metal in both cases makes them of interest. No attempt was made to determine the metallic element causing the dermatitis.

PITYRIASIS ROSEA: A CONTAGIOUS OR INFECTIOUS DISEASE?

William R. Hill, M.D., Boston

Two men, J. P. and R. T., were examined in the office of Dr. John G. Downing on Jan. 2, 1940. Both of these men were employed by the same firm as "carbon machine operators" and worked at adjoining machines. J. P. had an eruption of six weeks' duration and R. T. one of three weeks' duration. For both an unequivocal diagnosis of pityriasis rosea was made.

Although one is inclined to believe that this observation is mere coincidence, I feel that it is worth while to report suspicious cases of possibly contagious pityriasis rosea. Of more importance is the suggestive incubation period in the case of the second patient and the interesting industrial question which is raised.

Curiously, the next patient to be examined on January 2, Miss M. K., also had pityriasis rosea. Inquiry from other sources revealed that pityriasis rosea was unusually prevalent and unseasonable in New England the winter of 1940-1941.

520 Commonwealth Avenue.

Correspondence

ULCERATIVE REACTION FROM GENTIAN VIOLET IN THE TREATMENT OF IMPETIGO CONTAGIOSA

To the Editor:—Dr. Leon Goldman described an ulcerating process resulting from the use of gentian violet in a case of impetigo contagiosa (Ulcerative Reaction from Gentian Violet in the Treatment of Impetigo Contagiosa, ARCH. DERMAT. & SYPH. **42**:1122 [Dec.] 1940). Dr. Henry D. Niles, supplementing these observations (Ulcerative Reaction to Medication for Impetigo, ibid. **43**:160 [Jan.] 1941), reported the same reaction following the use of a 3 per cent solution of cupric sulfate. He interpreted the phenomenon as being caused by either a dermonecrotic strain of bacteria or a damming-up of the exudate due to the thick adherent scale produced by the medication.

Another interpretation may be suggested, especially on a clinical basis, by the following observations.

Recently I observed a case similar to the one Dr. Goldman described. One of the interns at the clinic treated a child whose eruption had been diagnosed as "ordinary impetigo" with a 3 per cent solution of gentian violet in 10 per cent alcohol. Several days later this patient was seen by me. At that time, in addition to the ulcerated lesion reported by Dr. Goldman and Dr. Niles, I also observed swelling and edema of the cheek and small peripheral satellite vesicles, typical of herpes simplex. The intern was uncertain as to whether these had been present previously. There was a slight lymphadenopathy on the affected side. The mother volunteered the information that the child was recovering from a severe "head cold" and had complained of some pain and tenderness in the affected cheek.

In view of this observation it may be suggested that in some cases the so-called ulcerative reaction to medication was possibly an example of herpes simplex. The differential diagnosis of this condition is at times difficult, especially when the eruption has been modified by injudicious or inadequate local therapy. The tendency of herpes simplex in certain cases to progress to ulceration with subsequent scarring is too well known to dermatologists to require further comment.

CHARLES KEMM GOOD, M.D., New York.

IMPETIGO

To the Editor:—As one who had the privilege of listening to the late Dr. Sabouraud, I should like to make a few remarks about the article by Dr. Stephan Epstein on staphylococcic impetigo contagiosa (ARCH. DERMAT. & SYPH. **42**:840 [Nov.] 1940).

Sabouraud described the primary lesion of impetigo as a short-lived, rarely visible bulla. Dr. Epstein describes the primary lesion of streptococcic impetigo as a vesicle and considers a bulla to be the primary lesion of staphylococcic impetigo.

Sabouraud includes among the various forms of impetigo one which he names bullous impetigo and which he identifies with impetigo contagiosa of Tilbury Fox. He writes:

"In some cases impetigo infects all the members of a family. This is bullous impetigo (impetigo contagiosa of Tilbury Fox). All impetigos are contagious but this form is more so than the others. All impetigos are bullous, but this is the

only form which shows bullae, occasionally giant-sized, visible from the start. This impetigo is invariably epidemic. All who come in contact with the first patient are infected. As in all other impetigos a well directed treatment brings rapid cure, and by the same methods, although with somewhat more difficulty" (Maladies du cuir chevelu, Paris, Masson & Cie, 1932, p. 49).

Dr. Epstein declares that he has never seen streptococcic impetigo turn into staphylococcic impetigo but that he has seen apparent staphylococcic lesions assume the picture of streptococcic impetigo. This is exactly contrary to the opinion of Sabouraud, many times repeated and emphasized, that the primary bullous lesion of impetigo is invariably contaminated with staphylococci, which are always found in the crust of impetigo. In cases of this kind the staphylococcus is always a secondary invader, never a primary one. In addition, Sabouraud states that the streptococcus never takes second place to the staphylococcus and is never a secondary invader of lesions caused by the staphylococcus. As he expresses it, the staphylococcus possesses more rustic manners than the streptococcus and easily makes itself at home in the presence of the streptococcus.

Sabouraud was well aware of the existence of circinate impetigo in the adult. He has a picture of a patient with this condition on page 510 of the aforementioned text. He describes the lesions as having thinner, flatter, more pasty crusts than those of impetigo in the child. The lesions are resinous (varnish like) and never honey colored. This apparently is the staphylococcic impetigo described by Dr. Epstein.

I should like to offer a simple explanation of the connection of pemphigus neonatorum with the streptococcus. As all streptococcic lesions are invaded by staphylococcus, should the latter be particularly virulent, it may give rise to other primary lesions on its own responsibility. As the streptococcus in turn never invades primary staphylococcic lesions, staphylococci are recovered in pure culture from lesions of pemphigus neonatorum. The original point of departure may lie in an unnoticed streptococcic impetigo, either in the patient with pemphigus neonatorum or in any person in contact with him.

SEYMOUR J. WHITE, M.D., Lawrence, Mass.

Obituaries

HENRY E. MENAGE, M.D.
1872–1940

Dr. Henry E. Menage died on Oct. 23, 1940 at his home in New Orleans. He was 68 years old and had retired from active practice and teaching. He was a graduate of the Tulane University of Louisiana School of Medicine. On the outbreak of the Spanish-American War he became an officer in the Medical Corps of the United States Army. He served in the Philippine Islands in active and difficult campaigning. After the war he studied dermatology in Paris and on his return to New Orleans made diseases of the skin his specialty. He was a member of the Founders' Group of the American Board of Dermatology and Syphilology. He taught in the department of dermatology of Tulane University of Louisiana School of Medicine and became head of that department. He was also chief of the service of dermatology in the Charity Hospital and consultant to the Eye, Ear, Nose and Throat Hospital and the Illinois Central Hospital. He was frequently called in a consulting capacity to many public and private institutions in New Orleans.

Dr. Menage's private practice was large and covered a wide area in Louisiana and the adjacent states. Scrupulously conscientious in the care of his patients he had their full confidence in his professional ability and good judgment.

Among his colleagues, many of whom have been his pupils, the impression which survives his death and which will endure is that he was a keen observer, an able clinician and an excellent teacher. He is remembered by the medical profession not only for his medical skill and for his integrity but also for his strong personality and a charm of manner that endeared him to his associates.

R. H.

News and Comment

EXAMINATION FOR CERTIFICATION BY THE AMERICAN BOARD OF DERMATOLOGY AND SYPHILOLOGY

A written examination will be held on November 3. Applications must be received by the secretary, Dr. C. Guy Lane, 416 Marlborough Street, Boston, by September 23.

An oral examination will be held on Dec. 12 and 13, 1941. Applications must be received by the secretary by November 8.

DEATHS

Dr. George H. Belote, Ann Arbor, Mich., died on March 11.
Dr. Andrew J. Gilmour, New York, died on March 9.

Abstracts from Current Literature

EDITED BY DR. HERBERT RATTNER

SCLEREDEMA ADULTORUM. PAUL A. O'LEARY, MORRIS WAISMAN and MALCOLM W. HARRISON, Am. J. M. Sc. **199**:458 (April) 1940.

The authors review a group of 15 cases of scleredema adultorum. In all but 3 the initial symptoms were preceded by an acute infectious disease. Amelioration of the disease followed the removal of septic teeth or tonsils in several instances. Thyroid medication was thought to have little value. The best results were obtained with induced fever and the use of radiant heat, ultraviolet irradiation and judicious massage.

ADIE'S SYNDROME: A NON-LUETIC DISEASE SIMULATING TABES DORSALIS. JOHN MCDOWELL MCKINNEY and MAURICE FROCHT, Am. J. M. Sc. **199**:546 (April) 1940.

McKinney and Frocht report that Adie's syndrome is not rare and is probably frequently overlooked or confused with syphilis. It is characterized by a tonic pupil, the loss of one or more deep reflexes and frequently the unilateral absence of the ankle jerk. It is not due to syphilis.

THE COST OF SYPHILIS. JOHN STOKES, HERMAN BEERMAN and NORMAN INGRAHAM, Am. J. M. Sc. **199**:586 (April) 1940.

Stokes, Beerman and Ingraham review the monetary cost of syphilis in order to gain insight into the need for effective control of the disease. The total cost of syphilis is enormous and well justifies continued and even increased expenditure by various governmental agencies so that adequate and early treatment may reduce the cost of later stages of the disease. The authors record the estimates of various writers as to the cost of syphilis for a person treated in private practice. These figures range from $300 to $1,000 or more for one year of treatment by general practitioners or specialists. While these estimates may be accurate for certain communities, there must be numerous localities where the best available private treatment can be obtained for a great deal less than these amounts. It may be unwise to allow the public (and the government) to gain the impression that such large fees are the rule rather than the exception.

REGULATION OF CIRCULATION IN THE SKIN AND MUSCLES OF THE LOWER EXTREMITIES. MAE FRIEDLANDER, SAMUEL SILBERT and WILLIAM BIERMAN, Am. J. M. Sc. **199**:657 (April) 1940.

The authors employed seven different methods to alter the circulation in the lower extremities. Their observations indicate that the circulatory response is not necessarily parallel in the skin and muscles. Only one method, the intravenous injection of hypertonic solution of sodium chloride, increased the circulation in both superficial and deep structures. Ganglionectomy, with the resulting sympathetic paralysis, has no physiologic basis in the treatment of intermittent claudication, for circulation in the muscles is not increased even though the temperature of the skin may be raised. On the other hand, when ulceration is present one should employ a method of treatment which will increase the circulation of the skin.

CORONARY EMBOLISM: A COMPLICATION OF SYPHILITIC AORTITIS. WILLIAM B. PORTER and EDWIN W. VAUGHAN, Am. J. M. Sc. **200**:184 (Aug.) 1940.

Although the coronary arteries are frequently occluded by thrombosis, occlusion by embolus is rare. The pathogenetic mechanism is composed of: mesaortitis in the proximal portion of the aorta, atheromatous changes in the intima, mural thrombi attached to these plaques and emboli from these thrombi causing occlusion of the left coronary arteries, with sudden death. Porter and Vaughan thus add a fourth complication to the three classic manifestations of syphilitic aortitis.

COMPARATIVE STUDY OF THE BOERNER-LUKENS COMPLEMENT FIXATION TEST. ROBERT A. KILDUFFE and DORIS B. DAVIS, Am. J. M. Sc. **200**:249 (Aug.) 1940.

The Boerner-Lukens complement fixation test offers the advantages of rapidity and technical simplicity (*Am. J. Clin. Path.* **9**:13, 1939). Kilduffe and Davis report the results of this method in a comparative trial of 1,000 routine serologic tests at Atlantic City Hospital along with those of the Kolmer and Kline tests. The new test gave a larger number of positive reactions than either of the older methods. The number of strongly positive reactions was greater with the Boerner-Lukens test, while the weakly positive reactions were more definitely shown by the Kolmer test.

The authors believe that the Boerner-Lukens test possesses a degree of sensitivity and delicacy warranting its inclusion among the procedures acceptable for general use in the serologic study of syphilis. They recommend it particularly for laboratories which have previously omitted complement fixation tests for reasons of economy.

CERTAIN FACTORS GOVERNING THE INCIDENCE OF CEREBRO-VASCULAR CRISES. DANIEL L. DOZZI, Am. J. M. Sc. **200**:259 (Aug.) 1940.

Dozzi has reviewed the protocols of 1,000 autopsies and the clinical records in order to determine the factors which govern the occurrence of cerebrovascular accidents. Meningovascular syphilis was the cause of only one of these accidents. Heart disease in general was a major etiologic agent. The proportion of patients having cardiovascular syphilis was about that having all types of heart disease. The incidence of cerebral lesions was apparently lower in the presumably syphilitic patients than in the remaining subjects. Dozzi thus concludes that syphilis is not a very important etiologic factor in cerebrovascular accidents.

THE PATHOGENESIS OF SYPHILITIC OPTIC ATROPHY. HENRY P. WAGENER, Am. J. M. Sc. **200**:280 (Aug.) 1940.

Wagener reviews the recent literature on syphilitic atrophy of the optic nerve. He points out that syphilis may involve the optic nerves in three ways: first, optic neuritis, which may result in secondary atrophy of the optic nerve; second, retrobulbar neuritis, followed by retrobulbar atrophy, and third, primary atrophy. Until recently it was thought that the gradual diminution of central vision and contraction of the fields were a result of diffuse involvement of the nerve (tabetic type); in cases in which the central vision remained normal while the fields contracted there was thought to be intracranial basal meningitis.

The author states that recent opinion based on pathoanatomic observations favors the conception that the atrophy is secondary to inflammation of the meninges or the nerve rather than a toxic or primary degenerative process. He also points out the facts in favor of the concept of atrophy as a toxic effect. The newer theories of the pathogenesis of atrophy of the optic nerve are also reviewed, as are the observations which make them untenable or unproved. Abadie regards the atrophy as a result of nutritional disturbance of the nerve due to syphilitic involvement of its blood supply. Others contend that the blood supply is inadequate because the retinal diastolic pressure is decreased. Still other observers contend

that arachnoiditis causes constriction of the nerves and their blood supply. On the basis of these observations, Wagener advises surgical intervention in cases in which the atrophy progresses in spite of modern antisyphilitic treatment. A fourth theory is that tabes and atrophy of the optic nerve are the result of combined syphilis and nutritional deficiency.

Throughout this review the author depends to a great extent on the recent papers by Moore and his co-workers. LYNCH, St. Paul.

THE UNTOWARD REACTIONS OF TRYPARSAMIDE. I. KOPP and H. C. SOLOMON, Am. J. Syph., Gonor. & Ven. Dis. **24**:265 (May) 1940.

The reactions to tryparsamide during the sixteen years from 1923 to 1939 following 43,308 injections given to 829 patients in an average dose of 3 Gm. are summarized and described. Visual disturbances occurred in 37 patients, appearing in 18 during the first five injections and in 29 during the first ten injections. Atrophy of the optic nerve occurred in 10 patients, but only in 2 was vision greatly affected. Nitritoid reactions occurred in 41 patients, in 31 of whom they occurred after 30 injections. Gastrointestinal symptoms occurred in 59 patients; 30 had jaundice; 8 had dermatitis, and 5 had urticaria. Cerebral symptoms and disturbances of the peripheral nerve were rare and not serious.

LIVER DAMAGE AFTER RECOVERY FROM POSTARSPHENAMINE JAUNDICE. T. J. RANKIN and F. W. MARLOW, Am. J. Syph., Gonor. & Ven. Dis. **24**:301 (May) 1940.

Sixty-two cases of syphilis in which jaundice developed during the administration of arsenicals from 1918 to 1938 are reviewed. Only 24 of these were studied as to symptoms and signs of hepatic damage, results of the bilirubin excretion test for liver function, serum bilirubin level, serum protein level, serum albumin-globulin ratio, urobilinogen level in the urine, red blood cell counts, mean corpuscular volume, hemoglobin concentration, roentgenographic findings in the liver and infra-red photographs of the anterior abdominal wall. No cirrhosis of the liver directly attributable to jaundice prior to the use of arsphenamine was found, and in 18 cases there was laboratory evidence of mild residual hepatic damage. In cases in which alcoholism was a factor the extent of abnormality was greatly increased.

ACUTE NECROSIS OF THE LIVER IN INFANTS FOLLOWING SODIUM BISMUTH THIOGLYCOLLATE ADMINISTRATION. I. J. WOLMAN, Am. J. Syph., Gonor. & Ven. Dis. **24**:330 (May) 1940.

Two cases in which acute necrosis of the liver followed the use of thio-bismol and caused death are reported. In neither case was the presence of congenital syphilis definitely established before treatment was begun. Patient 1 succumbed five days after the first and only injection of 0.032 Gm., and patient 2 had received fourteen injections of sulfarsphenamine and nine previous injections of thio-bismol. Death occurred two days after the tenth injection. In both cases the pathologic diagnosis after autopsy was acute necrosis of the liver. REUTER, Milwaukee.

DERMATOMYOSITIS AND SYSTEMIC LUPUS ERYTHEMATOSUS. HARRY KEIL, Arch. Int. Med. **66**:109 (July) 1940.

Keil describes 5 cases with symptoms and signs suggestive of both acute lupus erythematosus and dermatomyositis, illustrating a condition which he regards as "transitional." In 2 instances there was suggestive evidence that lead influenced the clinical picture. "It is suggested that lead may exert a deleterious effect on the blood vessels in especially susceptible persons with a presumably unstable vascular system and in such persons 'vascular disease may be and remain the solitary sign of lead poisoning.'"

EFFECT OF HIGH MELANOPHORE HORMONE FRACTIONS ON TYROSINE AND DOPA OXIDATION. G. A. FOSTVEDT, Endocrinology **27**:100 (July) 1940.

The information concerning the role of the melanophore hormone of the pituitary body in higher animals is meager. For this reason the author studied the effect on the hypophysectomized frog of injection of high melanophore hormone fractions obtained from beef and whales. Certain fractions accelerated the tyrosine-tyrosinase oxidation system, while others caused a decided decrease in dopa oxidation.

THE ACTIVATING, TRANSFORMING, AND CARCINOGENIC EFFECTS OF THE RABBIT PAPILLOMA VIRUS (SHOPE) UPON IMPLANTED TAR TUMORS. PEYTON ROUS and JOHN G. KIDD, J. Exper. Med. **71**:787 (June) 1940.

Rous and Kidd report further on their experimental studies on tumors. They review the effects of rabbit papilloma virus on implanted tumors, noting influences ranging from complete domination (change of the tumor to a virus papilloma) through hybrid variations to complete lack of effect. Since the rabbit papilloma virus influences tar cancers, they conclude that it must affect the cancers which derive from its own papillomas.

A TRANSPLANTABLE RABBIT CARCINOMA ORIGINATING IN A VIRUS-INDUCED PAPILLOMA AND CONTAINING THE VIRUS IN MASKED OR ALTERED FORM. JOHN G. KIDD and PEYTON ROUS, J. Exper. Med. **71**:813 (June) 1940.

A squamous cell carcinoma derived from a virus-induced rabbit papilloma has been propagated in fourteen successive groups of animals. The virus which originally changed a papilloma to this cancer has persisted and even increased, as evidenced by studies of antibody titer.

LYNCH, St. Paul.

THE EFFECT OF AGE ON THE SPREAD OF DYE IN THE SKIN OF NORMAL, ANTIGENICALLY STIMULATED, AND TUBERCULOUS GUINEA PIGS. R. Y. GOTTSCHALL and W. E. BUNNEY, J. Immunol. **38**:345, 1940.

The rate of spread of trypan blue in the skin of old normal guinea pigs is less than in young normal guinea pigs. The rate of spread of intradermally injected dye in old animals is not influenced by tuberculosis, but in young tuberculous guinea pigs it is retarded. Immunization with alum-precipitated toxoid does not influence the rate of spread of dye in young guinea pigs. The subcutaneous or intra-abdominal injection of dead tubercle bacilli into young guinea pigs retards the rate of spread of dye, as compared with the rate in young normal animals.

SULFANILAMIDE IN EXPERIMENTAL INFECTIONS WITH STREPTOCOCCI FROM SCARLET FEVER AND ERYSIPELAS. HELEN COOK NEWMAN, J. Immunol. **38**:377, 1940.

"1. A technic of sulfanilamide-therapy which was partially effective in protecting white mice against a strain of hemolytic streptococcus specific for erysipelas was ineffective in protecting them against a strain of hemolytic streptococcus specific for scarlet fever.

"2. No evidence of increased toxicity was found when sterile scarlet fever toxin in 1,000,000 skin-test-dose amounts was administered to mice treated with sulfanilamide.

"3. The addition of scarlet fever toxin to a culture of erysipelas organisms destroyed the effectiveness of sulfanilamide as a therapeutic agent in protecting white mice against a strain of hemolytic streptococcus specific for erysipelas.

"4. The effectiveness of sulfanilamide in protecting white mice against the two strains of hemolytic streptococci employed in these experiments was inversely proportional to the amount of toxin which was present in the culture or which was produced by the strain of hemolytic streptococcus used as the infective agent."

THE BACTERICIDAL POWER OF BLOOD FROM PATIENTS AND NORMAL CONTROLS FOR STAPHYLOCOCCI. WESLEY W. SPINK, JOHN R. PAINE and JEAN JERMSTA, J. Immunol. **38**:383, 1940.

The authors attempted to demonstrate the presence of antibacterial immunity in patients with staphylococcic sepsis. They evaluated the bactericidal power of whole defibrinated blood from patients and from normal persons for several strains of staphylcoocci. The killing power of the blood from 25 patients and from 18 normal persons was determined. Thirty-one strains of staphylococci were used, seventeen of them isolated from patients included in this report. All the strains proved to be pathogenic, according to the results of one or more tests for pathogenicity. The blood of both patients and normal controls possessed little or no killing power for the seventeen strains isolated from the patients. In some instances an appreciable number of organisms from heterologous strains were killed by the blood of patients and of normal controls.

POLYSACCHARIDES OF BLASTOMYCES DERMATITIDIS. ROBERT L. PECK, DONALD S. MARTIN and CHARLES R. HAUSER, J. Immunol. **38**:449, 1940.

Chemical analysis of *Blastomyces dermatitidis* indicates that this fungus contains at least two distinct polysaccharides.

"Minute quantities of these polysaccharides fix complement with sera prepared by immunizing rabbits with whole *Blastomyces dermatitidis*.

"Patients with American blastomycosis who are in the allergic state of the disease respond to intracutaneous injection of the polysaccharide with a swelling which reaches its maximum within 24 hours.

"Experience with one patient has shown that intravenous injection of a solution of this polysaccharide not only results in a decrease of carbohydrate sensitivity but also abolishes the sterile abscess-formation produced in an allergic patient by injection of heat-killed whole organisms."

ANALYSIS OF THE TUBERCLE BACILLUS AND ITS NATURAL PRODUCTS BY IMMUNE, ALLERGIC AND ANAPHYLACTIC TESTS. H. J. CORPER, J. Infect. Dis. **66**:23, 1940.

"On a simple synthetic non-protein medium (Wong-Weinzirl, 500 cc.), maximum bacillary growth of human tubercle bacilli occurs within two to three months, while tuberculoprotein liberation into the medium takes place mainly after maximum growth is attained.

"The bacillary body sensitizes primarily to tuberculo-allergy and serves to immunize against virulent infection, while the natural filtrate containing tuberculoprotein sensitizes to anaphylaxis and provokes anaphylactic shock and allergic intoxication but does not sensitize to allergy nor specifically immunize against virulent infection.

"Tuberculo-anaphylaxis, tuberculo-allergy, and tuberculo-immunity show distinctive characteristics which lead to the conclusion that they are separate and apparently unrelated biologic phenomena."

THE LOCAL FORMATION OF ANTIVACCINIAL ANTIBODIES BY THE SKIN. GEORGE HARTLEY JR., J. Infect. Dis. **66**:44, 1940.

"Intradermal inoculations of aluminum hydroxide gel cause the mobilization of cells consisting almost entirely of macrophages which are capable of phagocytosing the gel.

"When small quantities of vaccinia virus (testicular or neural strains) are adsorbed to aluminum hydroxide gel and are inoculated into tissues in which large numbers of macrophages are present, neutralizing antibodies are often demonstrable in extracts of this tissue before they are present in the undiluted blood serum or in other tissues.

"Inasmuch as this tissue consists predominantly of macrophages capable of ingesting aluminum hydroxide gel to which the virus has been adsorbed, the conclusion seems warranted that these neutralizing antibodies are produced by the macrophages in this area."

STUDIES ON THE INFECTIVITY OF VACCINAL ELEMENTARY BODIES. DOUGLAS H. SPRUNT, WALTER MARX and J. W. BEARD, J. Infect. Dis. **66**:53, 1940.

The authors studied the relation of infectivity to the elementary bodies of vaccinia in purified suspensions, injecting purified vaccine lymph into rabbits.

"Under the conditions of the experiments, an average of 366 bodies behaved as an infectious unit. On the other hand, in all experiments, the frequency distribution of positive and negative inoculations with the successive dilutions of elementary body suspensions followed the curve to be expected if a single elementary body is capable of inducing a lesion. The value 366 was obtained under a given set of practical conditions with respect to the strain of elementary bodies, the volume of inocula and sampling of test rabbits. It should be emphasized that the observed infectivity of vaccinia virus is more than a little dependent on experimental conditions. The possibility exists that under ideal circumstances a single elementary body may behave as an infectious unit." CORNBLEET, Chicago.

SOME OBSERVATIONS ON THE SUGAR METABOLISM IN ACNE VULGARIS, AND ITS TREATMENT BY INSULIN. HENRY C. SEMON and FRANZ HERRMANN, Brit. J. Dermat. **52**:123 (April) 1940.

A study of the blood sugar tolerance curves of 11 patients with acne showed in 9 of the cases (7 women and 2 men) a delay in sugar assimilation. Estimations were made at least twice and in some cases three or four times. In 5 of the women there was an exaggeration of the "lag" at the beginning of menstruation. These patients were treated with insulin—protamine zinc insulin in some cases and ordinary insulin in others—the dosage varying in each instance and depending on the degree of sugar tolerance and the effect on the acne lesions. In all cases the results without local treatment have been "consistently encouraging." When the treatment was interrupted, relapse was the rule, followed by renewed improvement when treatment was resumed. In some of the women the insulin caused either earlier or later menstrual termination, and in others cycles previously irregular became regular. The authors state the belief that in cases of acne the carbohydrate metabolism is not the only point at which insulin is operative and also that it probably prevents an excessive pituitary (basophil cell) effect. But for the present they leave the question open as to whether the disturbance of sugar metabolism favors the development of acne lesions by increasing the sugar in the tissues, thus promoting growth of pyococci, or whether there is an additional relation between the hormone abnormalities and the skin (sebaceous adnexa) which may be corrected by the administration of insulin.

COLLIERS' STRIPES—THE COAL-MINERS' DERMATOSIS. F. RAY BETTLEY, Brit. J. Dermat. **52**:129 (April) 1940.

Colliers' stripes appear on exposed parts as numerous linear and irregularly shaped marks, the result of accidental tattooing of coal dust into the skin. It has been claimed that these wounds rarely suppurate and that the particles of coal do not excite any reaction in the tissues. Bettley's observations disagree with these. Suppuration occurs no less than is to be expected, and histologically he has found a foreign body reaction, particularly near blood vessels. RATTNER, Chicago.

Society Transactions

SAN FRANCISCO DERMATOLOGICAL SOCIETY

FRANCES TORREY, M.D., *Chairman*

H. V. ALLINGTON, M.D., *Secretary-Treasurer*

April 19, 1940

A Case for Diagnosis (Dermatitis Medicamentosa Due to Phenolphthalein?). Presented by DR. NORMAN N. EPSTEIN and DR. ERVIN EPSTEIN, Oakland, Calif.

D. R., a white man aged 62, had a moderately pruritic and burning eruption on his face, neck and upper extremities which developed about four months ago. He works in a pickle factory. For several years he has been taking a laxative containing phenolphthalein once or twice monthly. He has had no diarrhea or sore mouth.

Examination reveals a strikingly symmetric eruption on the face, neck, arms, forearms and back of each hand, consisting of discrete dull red erythematous patches. There is some pigmentation. The lesions of the face are extensive and diffuse. On the arms and forearms they involve the greater portion of the lateral surfaces. There is a fading herpes zoster on the right flank. The results of physical examination were otherwise essentially normal. The blood count and the urine were normal.

DISCUSSION

DR. HARRY E. ALDERSON: This condition looks to me like solar sensitivity. The lesions on the wrists look different from the others; they are largely vascular.

DR. MERLIN T.-R. MAYNARD, San Jose: I considered this case possibly one of contact dermatitis. I do not know whether any of the chemicals used in pickling are likely to produce solar sensitivity. I think that the patient should be given patch tests with pickling substances.

DR. H. J. TEMPLETON, Oakland, Calif.: I suggest the diagnosis of acute lupus erythematosus.

DR. ERVIN EPSTEIN, Oakland, Calif.: I saw the patient only once. I thought the lesions were those of erythema multiforme. The fact that he was taking phenolphthalein twice a month made me suspect that phenolphthalein was the etiologic agent.

DR. NORMAN N. EPSTEIN: In regard to acute lupus erythematosus, the patient has had no constitutional reaction and his blood count is normal, which would not seem to fit in with that diagnosis.

A Case for Diagnosis (Syringomyelia?) Presented by DR. F. G. NOVY JR., Oakland, Calif.

D. Y., a laundress aged 24, came to the clinic of the University of California Hospital with chronic painless ulcers on the left sole. She had loss of sensations of pain and temperature in stocking distribution below both knees. This condition has been recurring on both feet and toes for the past six years. It starts with blisters and is frequently accompanied by lymphangitis and inguinal adenopathy. A similar condition had been present in the paternal grandfather, the father and 1 of 3 sisters.

The patient has been hospitalized at the State University Hospital in Oklahoma City, the Los Angeles County Hospital and the University of California Hospital.

Diagnoses have included Buerger's disease, Raynaud's disease, status dysraphicus lumbosacral syringomyelia and chronic progressive hypertrophic polyneuritis (Dejerine-Sottas disease).

Roentgenograms taken in March 1940 showed chronic osteomyelitis of the metatarsal bones of the left foot, together with a periosteal thickening of the tibia and fibula similar to the osteoarthropathy associated with chronic pulmonary disease. Roentgenograms of the chest were normal. The results of all laboratory studies were essentially normal.

DISCUSSION

DR. G. V. KULCHAR: The neurologic picture and cutaneous lesions are typical of syringomyelia.

DR. ERVIN EPSTEIN, Oakland, Calif.: The patient states that 4 members of her family have the same condition. There are changes in the bones on gross examination. The cutaneous lesions are merely trophic ulcers. This combination is suggestive of the syndrome called "familial osseous atrophy."

DR. G. V. KULCHAR: The changes in the bones may occur in association with syringomyelia.

DR. A. E. INGELS: I should like to ask whether the patient has been investigated from the standpoint of leprosy. I observed many cases of leprosy which started in a similar way at the Kalihi Receiving Station in Hawaii, but the conditions were more indurated.

DR. F. G. NOVY JR., Oakland, Calif.: The possibility of leprosy in this case has been pretty well ruled out, I think. Smears have been negative. With that much involvement, one should find involvement of nerves, which appear to be normal. I think this case is one of syringomyelia.

Rhinoscleroma. Presented by DR. J. M. GRAVES.

M. M., a Mexican housewife aged 50, was seen at the clinic of the University of California Hospital in 1934. A diagnosis of rhinoscleroma was made and confirmed by histologic examination of material from the nose. At that time the foul-smelling discharge from the right ear was attributed to the rhinoscleromatous process.

The patient showed almost complete occlusion of the anterior nares in 1936. At present the process is in an active phase. There are nodules on the lateral sides of both nasal vestibules, with occlusion of the nares on both sides. There is a decided diaphragming of the palate.

The patient has been followed in the clinic for fifteen years because of hypertensive cardiovascular disease. Prior to that she lived in Mexico.

DISCUSSION

DR. HARRY E. ALDERSON: Clinically the lesions are typical of rhinoscleroma. I saw some Mikulicz cells in the section. I heard recently from Dr. Estaban Reyes, of San Salvador, about some work he has done. The Frisch bacillus in his opinion is not the causative organism. He now thinks rhinoscleroma is a virus disease. He gives his reasons for this in a paper that will be published soon, in which excellent results of treatment based on this theory are reported.

DR. G. V. KULCHAR: Another condition that is similar to this is rhinosporidiosis.

Papulonecrotic Tuberculid. Presented by DR. H. E. MILLER.

L. C., a white woman aged 37, was first observed at the clinic of the University of California Hospital in October 1939, complaining of pain and swelling of both wrists. She gave the following history:

In 1930 she had cellulitis of the fingers, with fever and with sores in the mouth and throat and on the abdomen. In 1934 she had pleurisy with effusion. Roentgenograms showed no tuberculosis. In 1938 pleurisy for four days marked the

onset of phlebitis of both legs. In March 1939 several painful indurated areas, 1 to 3 cm., appeared on the left leg and healed with pigmentation.

Physical examination in November 1939 revealed no tuberculous focus. On November 9 injection of a 1 to 1,000 dilution of tuberculin showed a positive reaction with fever and chills. An ulceration, 2 by 3 cm., appeared at the site of the injection, which healed with scar formation. On Jan. 2, 1940 the patient presented a deep pustule with a purplish areola on the tip of the fourth finger. This was followed by the formation of purplish papules, 1 cm. in diameter, on the lower part of the left leg. These became necrotic and healed slowly with scarring. Similar scattered papules have appeared on the fingers and palms. The patient has received local medication only.

DISCUSSION

DR. G. V. KULCHAR: I think that this condition is an example of so-called "focal reaction" in tuberculin therapy and is a good argument against the use of large doses of tuberculin routinely.

DR. MERLIN T.-R. MAYNARD, San Jose, Calif.: I do not think that a dilution of 1 to 10,000 would be considered a large dose. Routinely, do you give 1 to 10,000 or 1 to 1,000?

DR. H. E. MILLER: In the clinic a dilution of 1 to 1,000 is given. In some institutions 1 to 10,000 is used. I never could understand why there was such a large difference in the two doses. I think that 1 to 1,000 is generally used, but why should this amount be used or one tenth of it? Why not 1 to 2,500 or 1 to 5,000 dilutions?

DR. G. V. KULCHAR: I think much smaller doses than that should be used routinely.

DR. STUART C. WAY: Tuberculin dilutions of 1 to 1,000,000 have been suggested, but 1 to 10,000 seems to be the ideal dilution; certainly 1 to 1,000 is too concentrated.

DR. H. E. MILLER: This case has been of interest to me from three standpoints: (1) what may happen to an occasional patient when a 1 to 1,000 dilution of tuberculin is given; (2) the development of a papulonecrotic tuberculid after a gangrenous tuberculin reaction, and (3) what would be the physician's defense and the outcome if medicolegal action were instituted in such a case.

Arterial Embolism of the Buttocks Following Intramuscular Injection of Bismuth Subsalicylate. Presented by DR. EDWARD A. LEVIN.

M. B., a white woman aged 30, began treatment for latent syphilis at the clinic of the University of California Hospital in 1936. Previous intramuscular injections (fifty-two) of bismuth subsalicylate were well tolerated. On April 4, 1940 the patient received an intramuscular injection of bismuth subsalicylate with a 2 inch (5 cm.) needle. No blood was noted with aspiration. About 2 cc. of air was inserted after the injection. The patient did not complain of pain. The site was rubbed for a minute.

About fifteen minutes after leaving the clinic, the patient began to feel severe pain in the right buttock and radiating down the right leg. She went home, and about one hour later the skin over the right buttock became discolored, swollen and very tender. Treatment consisted of the application of compresses wet with hot saline solution.

She reported to the clinic on April 11, 1940, one week after receiving the injection. Examination revealed the skin over the right buttock to be ecchymotic, with extensive induration about the site of injection and with some peripheral indurated discolored areas. The central portion appeared dark and gangrenous. The patient was afebrile. Except for localized moderate pain and tenderness, there were no other symptoms. A complete blood count and the results of urinalysis were within normal limits. A roentgenogram of the chest was normal. Roentgenograms of

the right buttock showed considerable amounts of heavy metal distributed in linear fashion. Dry heat has been used.

DISCUSSION

DR. HARRY E. ALDERSON: I think this sort of accident can occur without any mistake having been made in technic. A case of this kind has great nuisance value and can cause much worry.

DR. EDWARD A. LEVIN: Local arterial embolism following an intramuscular injection is relatively rare. There are, perhaps, 30 cases reported in the literature to date. When the patient was first seen, there was some discussion as to whether the condition was actually a bismuth embolus in an artery or whether an artery had been torn, resulting in an arterial hematoma.

Tuberculosis Cutis Orificialis. Presented by DR. H. V. ALLINGTON, Oakland, Calif.

S. S., a Negro aged 32, entered the Alameda County Hospital on Dec. 23, 1939 because of nasal discharge and a tender weeping crusted ulceration of the nares and adjacent skin of the nose and upper lip. This began as a "cold sore" below the left nares about one year ago, which gradually spread. The nose has frequently been obstructed, especially the left side, and a thick whitish purulent nasal discharge has been present.

Examination reveals reddening, irregular thickening and in places erosion of the nasopharyngeal mucosa. There is an irregular punched-out ulceration of the posterior pharyngeal wall, roughly 1 by 1.5 cm. in diameter, with a granular base. The nares and skin over the tip and the alae nasi and the adjacent portion of the upper lip are superficially ulcerated. The floor of the ulceration is irregular, with granular and papillary projections studding it. A purulent exudate is present, and adherent brownish crusting occurs unless this is prevented by frequent cleansing. The margins are fairly abrupt. Redness and infiltration extend for 1 cm. beyond the border of the ulcer, and the follicular orifices in this area are patulous and filled with hyperkeratotic material and debris.

A blood count and the results of urinalysis were normal. Smears from the nose did not reveal tubercle bacilli or fungi. The Wassermann reaction was negative. Examination of the spinal fluid gave negative results.

Roentgenograms of the chest were interpreted as showing quiescent bilateral pulmonary tuberculosis. Sections of a biopsy specimen from the pharyngeal ulcer taken on entry showed tubercle bacilli. A specimen taken on Jan. 17, 1940 from the margin of the ulcer on the nose was reported as showing chronic inflammation with vesiculation.

Five or six weekly intramuscular injections of a bismuth compound as a therapeutic test for syphilis resulted in no benefit. Recently the administration of gold and sodium thiosulfate was begun. There has been no improvement beyond that due to cleaning up and controlling secondary infection by compresses soaked in boric acid or a 1 to 5,000 solution of potassium permanganate.

(Sections were presented.)

DISCUSSION

DR. H. E. MILLER: I should like to suggest the diagnosis of lupus vulgaris. I see no reason to make a diagnosis of tuberculosis cutis orificialis simply because some of the lesions are near the mouth. Apple jelly nodules and all the characteristics of lupus vulgaris seem to me to be present.

Angioma of the Breast. Presented by DR. F. G. NOVY JR., Oakland, Calif.

L. K., a girl aged 2 months, has had a lesion on the right breast since birth. This is 4 cm. in diameter, involves all of the nipple and areola and extends to the lateral aspect of the breast. The lesion is made up of angioma of both the superficial and the deep cavernous type. The patient is presented with the question of prognosis regarding the breast and therapy to be used.

DISCUSSION

DR. HARRY E. ALDERSON: I think the prognosis is excellent with radium therapy. I have obtained excellent results in a very large number of cases of this kind with repeated short treatments with filtered radium radiation.

DR. F. G. NOVY JR., Oakland, Calif.: I should like to ask what is the possibility of some serious trouble to the breast at puberty or pregnancy if radium therapy is given.

DR. HARRY E. ALDERSON: There should be no untoward effects if small doses of filtered radiation are given every few weeks for about six months.

DR. H. J. TEMPLETON, Oakland, Calif.: I should treat this lesion with fairly soft rays of radium. Especially, I would use 10 mg. half-strength glazed plaques and 0.5 mm. of brass or silver filtration for a period of two and one-half hours at about six week intervals.

DR. H. E. MILLER: I believe that when one sees a patient with a vascular nevus, the first thing to decide is whether it should be treated at all. Many of the lesions undergo spontaneous involution. I advise keeping this patient under observation for a while.

DR. MERLIN T.-R. MAYNARD, San Jose, Calif.: I should like to cite 2 instances in which such lesions went unchecked. One was the case of a Japanese child of 7 years, with a lesion the size of an orange that a year before had been the size of a quarter. Dr. Emil Holman has operated on that child four times and is just now beginning to think that he has control of the condition. The other case was that of a baby with lesions on the head, who had cerebral symptoms and died of compression of the brain by a huge hemangioma of the meninges.

In cases like the one presented, why not use roentgen rays instead of radium? Filtration with 1 mm. of aluminum may be used. I have treated patients in this way with good results. One may treat the superficial strawberry part of the lesion with radium afterward, if desired. Many patients with this condition are sensitive to roentgen rays.

DR. CHARLES ALBERT SHUMATE: I disagree with one of the discussers that these lesions disappear. It is the experience of my associates and me in Dr. Alderson's office that the younger the patient, the easier he is to treat and the better the final result.

DR. G. V. KULCHAR: There is a great deal of difference between the radiosensitivity of the tissue of the breast and that of the cavernous vessels. Low voltage roentgen therapy with 1,000 or 1,200 r in one dose might be given. I am sure this would make the lesion disappear.

DR. NORMAN N. EPSTEIN: Several of the pediatricians whom I know definitely claim that angiomas of this kind do not require treatment and that they disappear in a large majority of cases. I think that this patient is an ideal one to watch.

DR. STUART C. WAY: Filtration through brass seems indicated in the treatment of vascular nevi. Alumnium filtration is frequently followed by telangiectasia.

Lupus Erythematosus. Presented by DR. MERLIN T.-R. MAYNARD, San Jose, Calif.

W., a white woman aged 23, was presented previously in 1938. She first sought medical treatment July 1929 for a small spot under the right eye which was diagnosed lupus erythematosus. She was not treated at this time and was not seen again until a year later. General examination at this visit showed no foci of infection or tuberculosis, although she stated that an aunt had tuberculosis. She was given gold and sodium thiosulfate intravenously in ascending doses up to 100 mg. She responded slowly, and treatment was discontinued after four months, during which she received sixteen injections. The last six were given concurrently with injections of bismuth subsalicylate.

She remained well until September 1936, four months after she had been married. Examination again showed no foci of infection, and treatment with bismuth and

gold compounds was resumed. She became pregnant in November of that year. Bismuth and gold compounds were given coincidentally for eighteen weekly injections, and the gold compound alone was given for an additional four. Her condition cleared completely on this treatment, and she went through her confinement without trouble. She was not seen again until April 1938, when a far more acute and extensive form of the eruption developed.

Prior to this the lesions had consisted of two very small spots about 1 by 0.5 cm. in the malar areas. The new flare-up consisted of numerous discoid spots, all small and discrete. It was suspected that a disseminated form might develop. Quinine bisulfate was prescribed on April 12. She improved slightly. A physical examination gave normal results. Her blood count was normal except for a slight secondary anemia.

Alopecia areata and also herpes zoster developed in October. Both responded quickly to treatment. Triphal was given in 25 mg. doses for twelve injections. Sulfanilamide was given in full dosage for three days, without appreciable improvement. In July 1939 alopecia areata recurred but again responded quickly to treatment.

The lupus erythematosus has steadily become worse in spite of further treatment with the gold compound, both alone and with the bismuth compound. Small injections of neoarsphenamine were likewise not helpful. On March 14, 1940 she was given sobisminol mass. She is a little better now.

DISCUSSION

DR. MERLIN T.-R. MAYNARD, San Jose, Calif.: I presented this patient because she has exhausted all my therapeutic ability. She seems to be improving somewhat on sobisminol mass, which is a simple form of treatment. I have also considered the prolonged use of small doses of sulfanilamide.

She wears glasses, and I wonder whether the type of glass used is permitting passage of wavelengths of light to which her skin is sensitive. If a nickel-containing glass were used, this effect might occur. There is a possibility that predominantly ultraviolet rays are getting through.

DR. G. V. KULCHAR: Why was sulfanilamide given for only three days? So short a period of treatment hardly seems a fair trial.

DR. MERLIN T.-R. MAYNARD: The dose was large, and after three days I thought I would discontinue the administration for a while and observe the result.

DR. G. V. KULCHAR: Eighty grains (5 Gm.) a day may be given for two or three weeks if necessary.

DR. A. E. INGELS: I should like to point out that there is no atrophy whatever. Most of the lesions show a transparency which suggests colloid degeneration of the skin. Besides, since the patient has not responded to any form of therapy, I should like to suggest review of the diagnosis.

DR. H. E. MILLER: I had a patient some months ago with the same verrucous type of lesion. I gave her five intramuscular injections of a bismuth compound. She improved greatly after the injections, and I gave her sobisminol mass to take by mouth for one month. The eruption became more severe while she was taking the bismuth compound by mouth but improved again when the intramuscular injections were resumed.

Pseudoatrophoderma Colli. Presented by DR. ERVIN EPSTEIN, Oakland, Calif.

L. N., a white woman aged 30, was first seen on April 5, 1940, complaining of an asymptomatic eruption which made her neck seem "dirty." The lesions had started fifteen years previously on the sides of her neck and slowly spread until the present sites were involved. She has noted that the exanthem seems darkest just before and during her menstrual period and fades somewhat during the intermenstrual period. Vigorous washing also causes a lightening in the color. She has 2 sons, aged 8 and 10 years, neither of whom are similarly affected. During her pregnancies the eruption was quiescent, but during the postpartum interval the

lesions became darker and more widespread. The patient states that she always feels "cold." She is 5 feet 5 inches tall (165 cm.) and weighs 160 pounds (72.5 Kg.). There is no history of other members of her family being affected in the same manner. Her parents are Austrians, and there is no history of consanguinity.

The patient presents an indistinct, faint slightly discolored shiny macular eruption on the sides and back of her neck, her chest and the upper portion of her abdomen. The skin in the oval macules is thrown up into tiny folds running vertically. Areas of normal skin are interspersed in the affected locations. Scraping the lesions causes a branny exfoliation. The lesions show no clinical evidence of inflammation. There is but little tendency on the part of the eruption to follow the lines of cleavage of the body.

Scrapings from the lesions examined microscopically in warmed 20 per cent potassium hydroxide show no evidence of a fungous infection. Numerous local remedies, including one-half strength compound ointment of benzoic acid N. F., have failed to affect the eruption in any way.

DISCUSSION

DR. ERVIN EPSTEIN, Oakland, Calif.: This case was interesting to me for two reasons: It is a good example of the type of case that Frost and I reported (Frost, K., and Epstein, E.: Pseudoatrophoderma Colli in Sisters, ARCH. DERMAT. & SYPH. **40**:755 [Nov.] 1939). However, the eruption is much more extensive in this patient, involving not only her neck but practically all of her trunk. Second, of the patients with this condition whom I have seen, in 2 it started at the age of 14 and in 1 at the age of 15.

She gives the classic history of the condition becoming worse during her menstrual periods and after delivery but better during pregnancy. This makes me wonder whether the condition might have an endocrine basis, in which case estrogenic therapy might be of value.

Glomus Tumor. Presented by DR. H. J. TEMPLETON, Oakland, Calif.

The section of a tumor removed from the lateral surface of the thigh of a man aged 65 is presented.

The patient had noted a tender mass beneath the skin for many years. When I attempted to palpate the tumor, the patient shrank from having it touched. On inspection, it appeared to be a subcutaneous tumor the size of a marble. The skin over it was definitely bluish. Treatment was by excision.

DISCUSSION

DR. STUART C. WAY: A man of 60 with a glomus tumor on the flexor surface of the forearm whom I saw last fall acted in a similar manner and complained that the growth was extremely painful on pressure.

NEW YORK ACADEMY OF MEDICINE, SECTION OF DERMATOLOGY AND SYPHILOLOGY

GEORGE C. ANDREWS, M.D., *Chairman*

HERMAN SHARLIT, M.D., *Secretary*

Oct. 1, 1940

Dermatitis Venenata (Due to Underwear Shorts). Presented by DR. JOSEPH L. MORSE.

J. P., a man aged 41, presented from the Skin and Cancer Unit of the New York Post-Graduate Medical School and Hospital, has an eruption involving the

penis, scrotum, buttocks and thighs of one month's duration. The patient had bought eight pairs of new underwear shorts, and after wearing four pairs in a period of ten days he noticed itching of the penis. He continued to wear the underwear, and the penis and the scrotum soon became swollen, while the skin on the buttocks and the thighs was red and pruritic. On admission to the clinic on Sept. 13, 1940, he presented a dermatitis with severe swelling of the scrotum and penis and erythema of the buttocks, thighs and hips.

Reactions to patch tests made with the underwear shorts were positive. Eight controls gave negative reactions to patch tests with the same underwear shorts. Patch tests with adhesive plaster gave negative results.

DISCUSSION

DR. LOUIS SCHWARTZ: I had the opportunity of investigating the outbreak of dermatitis from wearing apparel in Canada and in the United States. It was first reported to the Public Health Service by Dr. Donald S. Mitchell of Canada. He first noticed such dermatitis in women who wore brassieres made from certain cotton materials. He had ascertained that it was caused by the finish of the material but wanted some help from the Public Health Service in determining the chemical which caused the dermatitis. I obtained samples of the ingredients in the finish from the maker and sent them to Dr. Mitchell for use in patch tests. Dr. Mitchell found that the ester gum in the finish was the actual cause of the dermatitis. Although the makers of the finish were not satisfied with this report, because they had sold millions of gallons of this material in the United States and no cases of dermatitis from wearing apparel finished with it had been reported in this country, the company cooperated whole heartedly in the investigation. I also at first wondered why cases of this kind had been reported only from Canada, but about this time reports commenced to arrive from physicians in the United States of cases of dermatitis caused by wearing of shorts. The directors of a large chain store reported that there were forty-three complaints against them for dermatitis from wearing a particular batch of shorts they had sold. Patch tests showed that the finish of the material was the cause, and investigation by the Public Health Service showed that it was the same finish which had caused the dermatitis in Canada.

About the same time reports of dermatitis from nylon stockings began to appear. About five years ago, when nylon was in the experimental stage, E. I. du Pont de Nemours and Company asked the Public Health Service to help investigate the new fabric as a possible cutaneous irritant. Tests on 200 persons showed that it was not more of a sensitizer or cutaneous irritant than ordinary silk or rayon. Therefore, my colleagues and I thought that the dermatitis reported from nylon stockings was not due to the nylon itself but perhaps to the same finish which caused dermatitis when used on the cotton goods. I went to Indianapolis, where the cases of dermatitis from nylon stockings had occurred, and found as a result of patch tests that the identical finish used on the fabrics in Canada had been used on the nylon stockings and was the cause of the dermatitis. The hosiery manufacturer stopped the use of this finish on hosiery and had no more trouble. The makers of the finish were convinced by this time that it was the cause of the dermatitis and withdrew it from the market for use on wearing apparel, but it is still used on fabrics not intended for wearing apparel.

The manner in which the Public Health Service carried on this investigation shows what can be done in persuading a manufacturer to withdraw a dangerous product from the market without giving the firm adverse notoriety. It also shows how the Public Health Service can cooperate with private physicians in determining the actual cause of an outbreak of dermatitis. No mention of the manufacturer's name or of the trade name of the fabric or finish was made in the report.

Another point this investigation brings out is that up to the present manufacturers have been able to sell to the public new fabric, new dyes and other wearing apparel without knowing their toxicologic or skin-irritating properties. In our article (Schwartz, L., and others: An Outbreak of Dermatitis from New Resin Fabric Finishes, *J. A. M. A.* **115**:906 [Sept. 14] 1940) my co-workers and I recom-

mended that tests for the irritative and toxicologic action of new chemicals and wearing apparel be made and outlined a method for performing such tests. This method, although not perfected, gives a basis for argument and for discussion so that the best method can be worked out whereby a manufacturer may test a new chemical or a new fabric which he wants to sell to the public and may know that it will be reasonably safe before putting it on the market.

It would be to the advantage of dermatologists if they could help in some way to compel manufacturers to have tests made, such as I have proposed, before new materials for wearing apparel are sold to the public. Then dermatitis from wearing apparel would not occur as often as it does now. A new field for dermatologists would be created: testing for irritants in fabrics and materials. I think this work would also save a considerable sum for insurance companies and retail stores, both in law suits and in nuisance settlements.

DR. MARION B. SULZBERGER: I second everything which Dr. Schwartz has said, of course, and I should like to discuss such cases from the dermatologic-morphologic viewpoint. I have observed several cases of dermatitis from stockings and from shorts and other wearing apparel, and there are, I think, several points of interest as far as the cutaneous manifestations and the course of the eruption are concerned. In some of these cases not only is there an ordinary contact dermatitis at the site of exposure but there have been distinct urticarial elements or even generalized multiform erythema, as well as morbilliform eruptions, distant from the point of contact. Sometimes there is no contact dermatitis or positive reaction to a patch test and just the generalized exanthem is present, and sometimes the cutaneous disease is accompanied by general manifestations. Not only are patients with this condition often sick, but they are sick for a long while, even many weeks after the last cutaneous exposure. I think these observations are important, not only in relation to this particular excitant but in other cases in which one thinks a substance can be exonerated because the dermatosis continues for a long time after the last known exposure to the particular agent or because the eruption is not the typical one of contact dermatitis.

Another point I want to bring out is in relation to the studies mentioned by Dr. Schwartz. The investigated material is still being sold. Even though the company has withdrawn the finish itself from the market, there must still be a considerable stock of finished materials on hand in some places. Therefore in all likelihood this type of dermatitis will continue to be seen for some time, until the stocks of the materials finished with this particular substance are exhausted.

Another point is that materials manufactured and sold to consumers for use in wearing against the skin require entirely different precautions, controls and preliminary types of tests than do materials not intended for such use. I think, moreover, that dermatologists who will be called on to assist in this type of testing when new materials are being studied for consumer use next to the skin should realize that no one can give a definite answer insofar as the innocuousness of such materials is concerned. All one can do is to find out whether in hundreds of persons the material tested produces sensitization or irritation or both. Often the percentage of incidence of irritation or sensitization is very small. For instance, although hundreds of thousands of pairs of stockings are sold, there may be only 1 or 2 persons who become sensitized. Therefore, the probability of finding 1 person sensitized if one tests only 100, 200 or 300 persons is not very great. The best that manufacturers can expect is that the reaction to preliminary tests, if positive, will show that a certain material or fabric or dye or finish should not be used in wearing apparel because it has sensitized 1 or 2 persons in 100. But just because a material has failed to sensitize or irritate in a series of 200 subjects or so does not mean it is safe. It means only that it is safe to proceed with the material to clinical tests on larger series and under trial conditions of actual consumer use.

DR. LOUIS TULIPAN: I happened to get some of the material to which Dr. Schwartz referred and in several cases performed patch tests but observed no reaction.

I take the reverse position from that of Dr. Sulzberger in reference to the urticaria he states accompanies some of these eruptions. I feel that it is the urticaria which is the underlying condition. In other words, many of the persons who have these eruptions have a vasomotor irritability, and the dermatitis is caused not by the material alone or by the chemical used but by some other factor which comes into play, such as friction or an underlying xerodermatous skin. This also applies to wool and silk. Many persons will not show a positive reaction to patch tests with wool or silk but will have a dermatitis if they wear the materials.

Dr. E. William Abramowitz: I can recall encountering my first case of this kind about a year ago. The patient presented a generalized erythematous dermatitis involving particularly the penis, scrotum and thighs, with fever and general malaise. I was not able to incriminate the shorts until recently, when I observed 3 patients with this condition in a short time. The last one I saw today was in Gouverneur Hospital. The patient had an extensive morbilliform eruption of the body and considerable edema and redness of the penis and scrotum, with a dermatitis of the thighs from adhesive plaster used to support his penis and scrotum. I have obtained no history of atopy in these cases, but there apparently is a predisposition to sensitization. Patients with a condition like this usually require hospitalization.

Dr. Paul Gross: In studying the sensitizing properties of other textile finishes, Dr. Kesten and I had occasion to make comparative tests with the material under discussion. Of 128 persons submitted to a five or seven day sensitization test, 6 (4.6 per cent) gave a positive reaction. Among 38 persons tested with a primary forty-eight hour patch test, 1 gave a positive reaction, although there was no history of a previous eruption in this man or of contact with the textile finish. All the patients who gave a positive reaction also showed a strong reaction to tests with adhesive plaster. I believe the incidence of sensitization in 4.6 per cent of tested persons is exceptionally high, and this, combined with the clinical picture, points to unusually strong allergenic properties of the resin used in the finish. This, on the other hand, proves that sensitization tests performed on several hundred persons may not give an absolute guarantee against allergic reactions but certainly will prevent the use of highly sensitizing materials. The positive reaction to adhesive plaster mentioned before suggests that the resin of adhesive plaster might have acted, by previous contacts, as a sensitizer to the textile finish. Only the fact that the wide use of adhesive plaster is confined in the majority of cases to small areas prevents a more frequent occurrence of severe reactions from it.

Dr. J. Gardner Hopkins: This incident strikes me as an interesting example of what so often happens in medicine. When one person recognizes a disease entity, every one begins to report cases, whereas they probably have been encountering such cases for a long time without recognizing the condition.

The first observations of dermatitis due to the textile finish in question were, as Dr. Schwartz has said, made by Dr. Donald S. Mitchell. He recognized most of the features brought out tonight, such as the associated sensitization to adhesive plaster. He published no report but did discuss the matter with his colleagues. I happened to attend the meeting of the Canadian Medical Association last June, and it appeared that since Dr. Mitchell had called their attention to this condition most members of the dermatologic section had encountered a number of cases in their own practice. I believe that was before any had been recognized in the United States. In their experience printed house dresses seemed the most frequent cause of the dermatitis.

In reference to nylon dermatitis, there is one thing I should like to ask Dr. Schwartz. The only example of that which I have seen was a curious type of eruption consisting of follicular papules which were intensely pruritic. Incidentally the patient, not I, made the diagnosis on the basis of a newspaper article which mentioned these papules as characteristic of nylon dermatitis.

DR. HERMAN GOODMAN: Has this gum resin been further recognized or identified chemically? Some of the sodium and potassium salts are becoming popular for commercial utilization today. Has any one resin or resin ester been identified?

DR. LOUIS SCHWARTZ: I should like to answer some of the questions that have been asked, because I can perhaps do so better than other members who have not had as active a part as I have had in this investigation. The first question was by Dr. Hopkins on the follicular type of eruption. That was the type of eruption most often seen in dermatitis from nylon hosiery. I suggest that the term "nylon dermatitis" not be used because it has caused the du Pont company a lot of trouble and the loss of a considerable amount of money. The dermatitis is not really due to the nylon in the hosiery but to the finish which was used on the nylon.

I did not speak about the symptoms of the dermatitis from these fabrics because they were well described in our article, but there were some points not brought out in the discussion this evening. In the cases I observed, and there were many of them, the dermatitis extended up the length of the leg and thigh to the point where the stockings ended but was not present below the ankle. That area was free from the eruption. My colleagues and I thought at first this was due to the fact that the part of the foot in the shoe was not exposed to the sun, but exposure to sunlight did not account for it because the part between the ankle and shoe top, which was exposed to the sun, was also unaffected. The stockings are sheer and loosely woven, and contact with the skin is not continuous. This may in some degree account for the follicular type of eruption; whereas in the case of shorts the threads are much closer together and the skin is in practically continuous contact with the fabric, and as a result the dermatitis from the shorts is a confluent type.

Dr. Goodman asked whether the actual irritant in the finish is known. It is glycerin abietate, an ester gum. Abietic acid is one of the principal ingredients of pine resin. Resin is used as the adhesive in adhesive plaster, and Dr. Peck and I some years ago proved that the resin was the principal irritant in adhesive plaster. In making glycerin abietate, or the ester gum, abietic acid is neutralized by combining it with glycerin. When it is completely neutralized it is neutral glycerin abietate. It is difficult to combine completely all the abietic acid; most ester gums are acid, and the degree of acidity is given by the acid number. The acid number of the ester gum may be high or low, depending on the amount of free abietic acid. The lower the acid number the less likely the substance is to be a sensitizer or cutaneous irritant. The glycerin abietate used in this finish had an acid number of 6—not very high—and dermatitis probably would not have resulted as frequently from the use of this ester gum in the finish if xylene had not been used as an emulsifying agent. In our investigations it was shown that traces of xylene were still present in the finish on the hose even after many months. This helped to hold the ester gum in solution and contact or wet the skin. A substance must wet the skin in order to act on it. Abietic acid and glycerin abietate are only very slightly soluble in water but are very soluble in xylene. I think the traces of xylene remaining in the finish on the hose helped to cause the dermatitis by holding the resin in solution so as to enable it to wet the skin.

Some one asked whether the fabrics retained their irritating powers after washing. One of the principal selling points in the introduction of these finishes on the market is that they will stick to the fabric even after washing. The purpose of the finish is to give selling appeal and certain other properties to the fabric. The finish will not serve all these purposes if it readily washes out. It is therefore made to stay on even after many washings. It is true that some of it is removed after the first washing, but some of the women wearing the nylon stockings still had positive reactions after washing the hose with soap and water. Therefore, ordinary washing with soap and water did not completely remove the finish.

DR. HERMAN GOODMAN: The abietates are being offered to cosmetic firms for new types of cosmetics. It might be well for those who have to do with cosmetics to remember the abietates. What is the differentiation between irritation and sensitization? Why must both terms be given at this late date?

DR. JOSEPH L. MORSE: It was because of Dr. Schwartz's timely article that I presented this case. I did not expect such a lengthy discussion. This man's reaction to a patch test which you saw tonight was not as severe or as intense as the reaction to the forty-eight hour patch test he had had previously. This patch was put on twenty-four hours ago because the other had nearly disappeared and I thought the members would like to see the positive reaction. He had no reaction to a patch test with adhesive plaster. Apropos of what Dr. Sulzberger and Dr. Abramowitz brought out, it has certainly been my experience too that the dermatitis caused by this finish is intense. The itching is severe and lasts for weeks after the patient has stopped wearing the article of clothing responsible.

A Case for Diagnosis (Dermatitis Seborrhoeica? Ariboflavinosis? Psoriasis?). Presented by DR. HENRY D. NILES.

J. F., a woman aged 46, a patient at the Skin and Cancer Unit of the New York Post-Graduate Medical School and Hospital, has had a more or less generalized eruption for about three years. It began on the hands and then spread to the areas behind the ears, under the breasts and in the groins and anal region. Since its onset at different times most of the body has been involved, including the scalp, axillas, back, arms, legs and feet. She has been treated with many topical applications, roentgen therapy, ultraviolet radiation and internal medications, which have included potassium iodide, inhalations of ethyl iodide, riboflavin, nicotinic acid, hydrochloric acid and six intravenous injections of metaphen solution. She has also been on a low carbohydrate and low fat diet.

There has been at most only some temporary relief.

Examination shows diffuse scaling of the scalp, a red, scaly eruption in and behind the ears and along the hair-skin border, redness and scaling of the eyelids and angles of the nose and lips, fissures at the angles of the mouth and a somewhat red, smooth and shiny tongue. There are red patches in the axillas, groins and intergluteal folds and small oval dry scaly patches on the sides of the trunk. There are some scaling and maceration between the toes. There are also red patches in the flexures of the elbows and three or four spots on the flexor surface of the right forearm. The skin of the thumbs and fingers shows erythema, scaling, induration and fissuring.

Examination of the scales from patches in several areas for tinea have always given negative results. The Wassermann reaction of the blood was negative. At one time the examination of the blood for sugar showed 190 mg. per hundred cubic centimeters and the urine gave a reaction for sugar. However, the urine has been sugar free for over a year with the patient on a suitable diet. On Feb. 7, 1940 the basal metabolic rate was + 7 per cent.

In spite of all treatment the eruption has not improved. Some areas are worse, and new lesions continue to appear. For the past six days she has painted the patches twice a day with 30 per cent precipitated sulfur in a 1 per cent aqueous solution of tragacanth. She is now taking 3 mg. of thiamine hydrochloride and two yeast cakes daily. The patient is presented for suggestions as to diagnosis and treatment.

DISCUSSION

DR. PAUL GROSS: The fact that this patient has been presented with several diagnoses in itself makes it worth while to investigate for vitamin deficiency. The absence of lesions on the mucous membrane of the lips speaks against ariboflavinosis. The appearance of the tongue suggests that cultures of material from the tongue and stools be studied for Monilia. I might mention that there is a close relation between systemic Monilia infections and vitamin B complex defi-

ciency, and I have seen extensive moniliasis of the skin disappear under treatment with vitamin B complex in the form of injections of liver extract. Further treatment with vitamin B complex and with its individual fractions may clarify the diagnosis in this case.

DR. HENRY D. NILES: The patient's mouth has improved somewhat with riboflavin. At one time she had a definite cheilitis, accompanied with severe scaling of both lips, and the tongue was more red and glazed than it is now. Ariboflavinosis, however, in my opinion does not explain the lesions on the hands, where the eruption started, or the most peculiar part of her eruption, the new lesions which have appeared lately on the flexor surfaces of the forearms. Two or three weeks ago there were no lesions on the flexor surfaces of the forearms, and three or four days ago she had none of the patches on the upper part of the back and around the clavicles which she shows tonight. That is the way her eruption has behaved for the several months since I have been observing her. The clinical picture changes considerably within a few weeks' time. At one time it definitely resembles psoriasis, while at other times it is like seborrheic eczema or moniliasis. Some of the lesions disappear without any treatment, either internally or externally. On the whole the disease has been most resistant to treatment. I had hoped to obtain more suggestions as to diagnosis and therapy.

DR. GEORGE C. ANDREWS: Have you treated this patient with liver extract?

DR. HENRY D. NILES: I have not tried liver extract.

Panniculitis (Lipogranulomatosis). Presented by DR. J. LOWRY MILLER.

L. G., a married Jewess aged 33, presented from Vanderbilt Clinic, complains of an eruption on the lateral aspect of the right thigh of one and one-half years' duration. The eruption began with a mildly tender red swelling on the lateral aspect of the right thigh. There was some fever, but no chills accompanied the onset. Shortly before the patient had had a tooth extracted. She had also been wearing a particularly tight girdle, the lower edge of which had rubbed the involved area. The lesion has gradually spread by the development of satellite lesions, which have gradually coalesced. Improvement followed a month's rest in bed and treatment with wet dressings.

Examination shows on the lateral aspect of the right thigh a considerably depressed, dusky red, warm, mildly tender area, measuring 10 cm. in diameter. The skin over this area is firm to the touch. There are several smaller satellite lesions measuring 1 to 2 cm. in diameter, scattered about the main lesion. The results of a general physical examination were otherwise normal.

The urine was normal. The Wassermann reaction of the blood was negative. The basal metabolic rate was —5 per cent. Examination of the blood showed 4,960,000 erythrocytes, 14.5 Gm. (100 per cent) of hemoglobin and 9,400 leukocytes, with a differential count of 52 per cent polymorphonuclear leukocytes, 33 per cent small lymphocytes, 11 per cent large lymphocytes, 1 per cent monocytes and 3 per cent eosinophils. Chemical examination of the blood showed 210 mg. of total cholesterol, including 54 mg. of free cholesterol and 156 mg. of cholesterol ester. Examination for evidence of endocrine disturbance gave negative results.

Histologic examination showed an epidermis with a slight hyperkeratosis and vesicular cells. The nuclei were surrounded by a clear space, the chromatin often being shrunken within it. The papillary and upper reticular parts of the cutis were the sites of increased cellularity and edema. This manifestation increased in intensity with the depth of the specimen. In the deep part of the cutis and subcutaneous fat there was a decided infiltration of round mononuclear cells. Areas of fibrous tissue proliferations were noted. This adipose tissue had undergone necrosis, and lipophages were present. There was a thickening of the vessel walls but no recognizable obliteration of the lumens of the large vessels. The changes were maximal in the fat tissue. Evidently the lesion was a granulomatous panniculitis.

DISCUSSION

DR. E. WILLIAM ABRAMOWITZ: This case is most unusual. I wonder if the presenter refers to panniculitis (Christian).

DR. J. LOWRY MILLER: Yes.

DR. E. WILLIAM ABRAMOWITZ: My impression is that the condition is a lipogranulomatosis. The patient gave a history of continual traumatism against a table, which may have caused an injury to the adipose tissue similar to that described in infants and designated as adiponecrosis subcutanea neonatorum.

DR. PAUL GROSS: Localized panniculitis has been separated in the literature from the recurrent febrile type of Weber-Christian disease. The separation is based on the clinical course more than on any histologic difference. Therefore, I suggest the diagnosis of localized panniculitis in this case.

DR. J. LOWRY MILLER: The patient does give a history of fever at the onset and also a history of vague attacks of what she calls "grip." At present she is getting over an attack of "grip." This morning she had a temperature of 100 F., and when she came to the hospital her temperature was 100 F. Also she has taken iodized salt over a period of two years. Some investigators think the halogen group has some etiologic relation. I am therefore going to have her stop taking iodized salt and see if there is any effect on the lesions.

Lupus Erythematosus and Lipogranulomatosis. Presented by DR. GEORGE C. ANDREWS.

W. L., a woman aged 34, was previously presented before the New York Dermatological Society on Nov. 28, 1939 (ARCH. DERMAT. & SYPH. **41**:965 [May] 1940).

There has been little change in the appearance of the lesions during the past year. Treatment has consisted of intravenous injection of gold sodium thiosulfate, injections of liver extract, calcium, iron cacodylate, sodium iodide, neoarsphenamine and acetarsone and application of filtered roentgen rays to the indurated lesion. The results of physical examination have been essentially normal. The blood count was normal; the Wassermann reaction of the blood was negative, and the urine was normal.

DISCUSSION

DR. HERMAN GOODMAN: It would be interesting to know if this woman was one of a series of patients treated about that time in the hospital with injections of a gold compound for lupus erythematosus. The gold compound was given locally at the site of the lupus erythematosus, and it was said to result in rapid cures.

DR. EUGENE F. TRAUB: The patient said she had had no local injections into the lesion on the face but had had only intravenous treatment.

DR. GEORGE C. ANDREWS: The patient was under my care for five years and had no local injections from me and none before she came to me.

DR. E. WILLIAM ABRAMOWITZ: Did you include muscle in the biopsy specimen, and if so, did the muscle show any special changes? I have observed many cases of lupus erythematosus, and I do not recall seeing these changes in any of them. I have seen conditions called lupus erythematosus that were really dermatomyositis.

DR. PAUL GROSS: May I ask the presenter how the differential diagnosis can be made in this case from lupus erythematosus profundus? As to the involvement of voluntary muscle in panniculitis, I believe the healed lesions with a total destruction of fat which stops at the fascia are against such an occurrence.

DR. GEORGE C. ANDREWS: Would Dr. Gross mind telling me what lupus erythematosus profundus is?

DR. PAUL GROSS: I remember a patient with lupus erythematosus profundus presented by Dr. Irgang at a dermatologic meeting last year. At that time I investigated the literature on that subject and found it extensive.

DR. MAURICE J. COSTELLO: S. Irgang (ARCH. DERMAT. & SYPH. **42**:97-108 [July] 1940) reported a case of lupus erythematosus profundus with clinical resemblance to Darier-Roussy sarcoid. I think that the condition of the patient under discussion resembles that of Dr. Irgang's patient.

Lichen Planus Spinulosus et Atrophicus (Lichen Planus et Acuminatus Atrophicus [Feldman]; Folliculitis Decalvans et Atrophicans [Graham Little]). Presented by DR. PAUL GROSS.

A. M., a housewife aged 58, is presented for Dr. Julius Raab. She was first seen at the Hospital for Joint Diseases in March 1939, at which time she had a typical eruption of lichen planus on the inner aspects of both knees. This cleared up under roentgen ray treatment. When the patient was seen again, in February 1940, she had an eruption of lichen planus on the hands, wrists and arms. She was given more roentgen ray therapy, to which the lesions again responded. About one week after the last treatment (June 1940) the present eruption appeared and has since spread. The condition of the scalp was noticed at about the same time.

The eruption at present consists of pinhead-sized follicular papules with barely perceptible inflammation and a central plug, which in many lesions forms a protruding spine. Most of the lesions are discrete, especially those on the backs of the hands, the upper and lower extremities, the chest and the abdomen. On the shoulders and back are large areas of closely cropped papules with very slight erythema of the involved skin. In the parietal region of the scalp are several patches of alopecia in which the skin is bluish red and somewhat thickened. The hair follicles are filled with whitish keratotic plugs. In several small areas the plugs and follicles have disappeared and the skin seems atrophic. On the inner aspect of the knees are pigmented spots which show the annular outline of the previous lichen planus, and the skin has a paper-like appearance. The mucous membranes of the mouth are free from lesions.

The Kline and Kahn reactions of the blood were negative. Histologic examination showed in one area a pronounced keratosis of the orifice of a follicle. The skin close to it showed the following changes: widening of the granular layer, pale large cells with a loss of spines in the spinular layer and a disappearance of the basal membrane. Underneath that part of the epidermis was a dense infiltration invading the epidermis and forming a small lacuna. These changes were suggestive of a follicular lichen planus.

DISCUSSION

DR. E. WILLIAM ABRAMOWITZ: Lichen spinulosus is linked with vitamin A deficiency (*J. A. M. A.* **114**:386 [Feb. 3] 1940). I had a case in which lichen planus cleared up under sodium arsenate and roentgen ray therapy and then a profuse lichen spinulosus eruption developed. The patient had eaten one meal a day for weeks and that was inadequate. I think that one should make inquiries along that line in other cases to determine the exact relation of vitamin deficiencies and various cutaneous disorders.

DR. MARION B. SULZBERGER: I was interested in Dr. Abramowitz' remarks. I do not think one has to look into the pediatric literature to find reports of a vitamin deficiency in this type of eruption. Dr. Naomi M. Kanof, Dr. Joseph Goodman and I for years, in many places in the literature, in discussions and in the year books, have called attention to the fact that in this type of case we have seen good results from large doses of vitamin A. We now treat patients with this condition with vitamin A concentrate regardless of their dietary history.

Dr. Goodman, of Boston, has had several complete cures from large doses of vitamin A. That means not that the cicatricial type of alopecia is cured but only that the folliculitis which is its precursor is cleared up. We now give as much as 500,000 or even 1,000,000 U. S. P. units of vitamin A daily, and in a few weeks the condition clears up. I suggest the members try it. I wish to say emphatically that just because a vitamin allays or cures a condition, it is not necessarily correct to conclude that the lack of the vitamin caused the particular disease. One is permitted to conclude only that large doses of the vitamin, doses many times above the daily requirement, in some cases produce alleviation or cure of some pathologic process which may or may not be due to local vitamin deficiency.

DR. PAUL GROSS: Every one is familiar with the history of this disease (McCafferty, L. K.: Folliculitis Decalvans et Atrophicans [Little], ARCH. DERMAT. & SYPH. **18**:514 [Oct.] 1928; Feldman, S.: Lichen Planus et Acuminatus Atrophicans, ibid. **34**:378 [Sept.] 1936). It was first described by Dr. Graham Little as a disease entity, but according to Dr. McCafferty, Dr. Little finally came to the conclusion that the condition was a variety of lichen planus. The occurrence of lichen spinulosus in this patient, whose lichen planus had healed, made it tempting to assume the duality of these two conditions. Careful study of the pathologic sections in this case, however, revealed changes in the epidermis and cutis around a follicular spine which were, to say the least, suggestive of lichen planus, so that the diagnosis of lichen planus spinulosus is justified.

The question of vitamin therapy in this case should be concerned first with the lichen planus. Recent reports speak of the favorable effect of nicotinic acid on lichen planus. I had occasion, a few months ago, to convince myself of the value of nicotinic acid in a case of generalized lichen planus. The presence of a combined deficiency in nicotinic acid as well as vitamin A would explain the combination of lichen planus and spinulosus. It will be interesting to see whether this patient will respond to nicotinic acid alone or will require additional treatment with vitamin A. I have been administering on an average 50,000 U. S. P. units of vitamin A per day with satisfactory results.

DR. GEORGE C. ANDREWS: Will you please tell what dose of nicotinic acid you have referred to?

DR. PAUL GROSS: In the case of generalized lichen planus I administered 50 mg. of nicotinic acid three times a day.

Incontinentia Pigmenti (Bloch-Sulzberger); Melanosis Corii Degenerativa (H. W. Siemens); Chromatophore Nevus (Naegeli). Presented by DR. J. GARDNER HOPKINS and DR. G. F. MACHACEK.

J. R., an American Negress aged 2 years, is presented from Vanderbilt Clinic with a generalized pigmentary cutaneous disturbance, which has been present since birth. It was observed for the first time on May 3, 1940, when the child was admitted to the pediatric service suffering from conjunctivitis, acute purulent otitis media, umbilical hernia and seborrheic dermatitis. She was later admitted to the Babies' Hospital for treatment of pyoderma and anemia.

Examination shows on the trunk, chest and extremities a peculiar irregularity of pigmentation which has resulted in a reticular and streaked pattern, best described as "marbling." This apparently results from an irregularity of hyperpigmentation so that brown areas are separated by black streaks. No evidence of any other congenital anomalies has been found.

Histologic examination of the skin showed that most of the epidermal cells had vesicular nuclei. A mild inflammatory reaction was present in the corium. This was expressed by a slight increase in perivascular cellularity and edema. There was also an increase of spindle cells. The pigment changes were striking. Sections stained with hematoxylin and eosin and Fontana's stain showed an increase of melanin in the epidermis. There were areas where several layers of epithelial cells above the basal layer contained pigment. Collections of chromatophores were

seen in some of the papillae and in the subepidermal reticular corium. In dopa-stained preparations, melanoblasts were fairly evenly distributed. It was concluded that the lesion represented a congenital anomaly of the pigment-producing epidermis (a kind of functional nevus). Hyperpigmentation evidently has been caused by the collections of chromatophores in the corium in these areas and not by increase in pigmentation of the epidermis. Other laboratory findings were not of consequence in relation to this condition.

A Negro child with incontinentia pigmenti.

DISCUSSION

DR. MARION B. SULZBERGER: I had little opportunity to examine this child or to go into the family history, but from the clinical appearance of the eruption, I think it is the most widespread and most typical example of incontinentia pigmenti I have seen. The case is also unusual because it is the first one reported of the occurrence of this condition in a Negro. I saw this condition in a Negro child presented by Dr. Oscar Levin (Naevus Reticularis et Pigmentosus, ARCH. DERMAT. & SYPH. **27**:141 [Jan.] 1933). This was the first incontinentia pigmenti I had ever seen in any one not a member of the white race. However, Dr. Levin's

patient had this condition in addition to the tuberculid for which the case was presented, and it was not presented as a case of incontinentia pigmenti. The present case is, therefore, the first case reported under this name with the patient a Negro. I did not see any other ectodermal defects, as described by Fraser, Hutner and me (Incontinentia Pigmenti [Bloch-Sulzberger], ARCH. DERMAT. & SYPH. **38**:57 [July] 1938), or any evidence of anything in the siblings as in the cases presented by Siemens and by Naegeli and by me. I think this case is so typical that no one here can fail to recognize this condition the next time he sees it.

DR. MAX SCHEER: I do not agree with the diagnosis of incontinentia pigmenti or with the other diagnoses with the lengthy Latin names. The case impressed me as one of a reticulated pigmented nevus. The child has had the condition since birth. I think the anglicized term, reticulated pigmented nevus, better explains what is seen than the other names which have been mentioned.

DR. G. F. MACHACEK: We were not cognizant of the fact that this case is the first reported instance of the condition in a Negro. I think Dr. Scheer is right. The lesion is a nevus and it is a pigmented nevus, but it is not a reticulated naevus pigmentosus. There are no nevus cells. It is a congenital anomaly, a functional nevus, if one likes. These pigmentary anomalies occur with many other conditions, not always in the same pattern and not always described as incontinentia pigmenti. There are two other names which are synonymous; it is also known as familial chromatophore nevus and has been called melanosis degenerativa by Siemens. I believe it is interesting in this case, as was brought out by Dr. Sulzberger, that there are no other congenital anomalies. There are apparently no congenital keratotic defects or central nervous system defects, such as Little's disease. In the first case which Dr. Sulzberger described there was a glioma with retinal degeneration. Of course there are anomalies and pigmentary dystrophy in some of the idiots. However, they are a little different. It is known that pigmentary anomalies occur with spina bifida. They are real nevi. Undoubtedly nerve defects are associated with pigmentary disturbances, as in Recklinghausen's disease, for instance, both hyperpigmentation and depigmentation are present. So, in fact, I think Dr. Scheer is correct. The lesion is a congenital, not a functional, condition of the pigment-producing apparatus and in that sense is a nevus, but it is a very special type of nevus in which apparently there are collections of chromatophores. The explanation of it is another matter. The changes are much the same sort one may find in cases of Addison's disease except that the distribution of the pigment and the patterns are different.

DR. MARION B. SULZBERGER: I agree with what Dr. Machacek has said. Incontinentia pigmenti is a rare form of nevoid anomaly. It is characterized by a histologic picture which is different from that of any ordinary cutaneous nevus. As Dr. Machacek brought out, there are no nevus cells but simply a heaping of the chromatophores, a sort of autogenous tattooing with the patient's own pigment in certain areas. That is what characterizes the process. I might differ about one thing which Dr. Machacek said, and that is about these changes being essentially the same as in Addison's disease. In Addison's disease I believe the dopa reaction is usually increased. In incontinentia pigmenti one sees no acceleration of epidermal pigment formation but merely a heaping of pigment visible to the naked eye through the skin and histologically a heaping of cutis chromatophores filled with pigment. The dopa reaction in incontinentia pigmenti is not increased at all. In contrast to Addison's disease, one can demonstrate no increase of epidermal pigment formation but simply an increase in the deposit of pigment in the cutis.

DR. J. GARDNER HOPKINS: May I ask Dr. Machacek one question? I thought the dopa-positive cells seemed very numerous in the areas over the clusters of chromatophores. Was that so?

DR. G. F. MACHACEK: I could not be sure. They were well scattered through the epidermis. There did not seem to be any particular relative increase from area to area. It did not seem to me that the epidermis was particularly hyper-

pigmented. From that standpoint, I think Dr. Sulzberger's criticism is well taken. In Addison's disease there is an increase in melanin in the epidermis.

DR. J. GARDNER HOPKINS: There is one other thing I should like to mention, which strikes one in looking at this patient or at the pictures of Dr. Sulzberger's patients. The pattern is unlike that of any other dermatosis. "Reticulated" is not a good adjective for it. There are little spider-like arrangements and fine wavy lines. I wonder if that can be due to the fact that this pigment is in wandering cells which may localize themselves along the lymphatic channels. I can think of nothing else that would explain this unusual pattern.

Ehlers-Danlos Syndrome. Presented by DR. BEATRICE M. KESTEN.

M. L. S., a Russian Jewish boy aged 3½ years, is presented from Vanderbilt Clinic. The patient has an involvement of the skin of the elbows and knees particularly and of the rest of the body to a lesser extent, which has been present since birth. The patient's birth was normal and his development has been normal. He bleeds easily from small cuts and scars easily. There is a tendency toward the development of black and blue spots on the extremities on slight trauma. The patient's grandfather had "a loose skin." The mother and father have negative Wassermann reactions.

The results of general physical examination are normal. The patient weighs 42 pounds (19 Kg.). There is obvious looseness of the skin, which is most evident over the larger joints. Over the patellas and tibias there are ecchymoses with thickening of the subcutaneous tissues and numerous scars. Similar areas are seen on the chin and elbows. There is a scar on the site of vaccination. There is also a slight increase of elasticity of the ligaments of the joints.

Examination of the blood showed 13.9 Gm. of hemoglobin (96 per cent), 7,900 white blood cells, 46 per cent polymorphonuclear leukocytes, 48 per cent lymphocytes, 4 per cent monocytes, 2 per cent basophils and 334,000 platelets. The red blood cells appeared normal. The patient's bleeding time was two minutes and clotting time four and one-half minutes. Tests for fragility showed that hemolysis began with a 0.425 per cent and was complete with a 0.3 per cent solution (same as control). Tests for capillary fragility showed no petechiae in three minutes at 40 mm. of mercury.

DISCUSSION

DR. HENRY D. NILES: An important feature in this case is the hyperextensibility of the joints. The child's fingers can be bent back dorsally. Because of the presence of the triad hyperextensibility of the joints, elastic skin and tendency to bruising over the joints, one can make a diagnosis of the Ehlers-Danlos syndrome.

DR. JACOB SKEER: It is my opinion that the condition in this case fits pretty well what is known as the Ehlers-Danlos syndrome (Skeer, J., and Kaplan, A. A.: Ehlers-Danlos Syndrome, ARCH. DERMAT. & SYPH. **42**:450 [Sept.] 1940). The patient has hyperelasticity of the skin and hyperextensibility of the joints, especially the small joints, such as those of the fingers and toes. There is fragility of the skin, as is evidenced by the numerous irregular atrophic scars on the forehead, elbows and knees. There are bruises and what are probably pseudotumors on the arms and forearms and on the anterior aspect of the legs. The typical tumors, which are wrinkled and have a raisin-like appearance, are not seen in the patient, but examination of the mother revealed such a tumor on the left elbow. I believe that the mother has the same condition.

Keratoderma Climactericum (Haxthausen). Presented by DR. JACK WOLF.

G. A., a woman aged 45, is presented from the Skin and Cancer Unit of the New York Post-Graduate Medical School and Hospital complaining of an eruption of the volar surfaces of the hands and feet of three months' duration. The family history reveals no abnormalities. The patient's parents and 3 children are living and well. There is no history of miscarriages. Aside from measles, the

patient has had no eruptions except for profuse sweating of the hands and feet since childhood. A sebaceous cyst was removed from the scalp seven years ago. Menstruation began at the age of 12 years and was regular and normal until the onset of menopausal changes a year ago. The last menstrual period occurred on June 5, 1940. There is no history of arthritis.

The present eruption started on the heels four months ago and spread gradually forward. At the onset it was painful, but later this was replaced by itching sensations. These patches never disappeared but spread progressively forward. The hands became involved about one month ago.

The patient is a healthy middle-aged woman of moderate weight (127 pounds [57.5 Kg.]) and height (59½ inches [151 cm.]). The pupils are equal and regular and react well to light and in accommodation. Examination shows on both palms, the right wrist and the dorsal surface of the proximal joint of the right ring finger several discrete, yellowish brown, well defined, slightly raised, irregular, nontender patches, from the size of a match head to that of an almond and larger, with fairly prominent slightly raised borders. On the palms the patches are distributed more along the thenar and hypothenar eminences. The fingers and the middle of the palms are free of any lesions. The nails are not involved. The trunk shows no lesions. There are lemon yellow, hyperkeratotic, diffuse, very thick, infiltrated patches involving almost the entire soles. They extend to both inner and outer surfaces of the feet to an area varying from ½ to 1½ inches (1.3 to 4 cm.), ending abruptly and forming a well defined zone with the normal skin. The central portions of the soles are of uniform lemon color and smooth. However, on the heels and at the bases of the toes the surface is rough and dark brown, with numerous fissures. There are extensive maceration and scaling between the toes with fissuring. The toe nails are not involved. There are several similar bean-sized to pea-sized superficial patches scattered alongside the dorsal surfaces of the first and little toes.

The results of urinalysis and chemical examination of the blood, the blood count and the basal metabolic rate were normal. The Wassermann reaction was negative. Examination of the urine for arsenic showed 0.02 mg. per hundred cubic centimeters of arsenic as arsenic trioxide and 0.18 mg. by volume.

The patient so far has received six injections of 2,000 international units of estrone (theelin) once a week, and local applications of 10 per cent salicylic acid salve. There has been no appreciable improvement as yet.

MINNESOTA DERMATOLOGICAL SOCIETY

CARL W. LAYMON, M.D., *President*

F. W. LYNCH, M.D., *Secretary*

St. Paul, Oct. 11, 1940

Lymphogranuloma Venereum. Presented by DR. J. F. MADDEN, St. Paul.

J. M., a Negro aged 26, stated that in 1929, while serving time in the West Virginia Penitentiary, he had homosexual relations with other inmates and a cauliflower-like growth developed around the anus. Six months later an inguinal bubo developed; this was incised, and a purulent material was expressed. There was no penile lesion at any time. During the past ten years he has been treated with many internal and external medications as well as with surgical excision. He was admitted to the Ancker Hospital in July 1940 with a right inguinal bubo, which had been incised, had receded and had recurred intermittently during the past ten years. There was a fungating mass surrounding the anus and extending anteriorly over the perineum. This mass was painful, had a foul odor and exuded pus. There was some narrowing of the anal orifice. The patient did

not improve after treatment with sulfanilamide but has improved appreciably after the administration of sulfapyridine (2-[paraaminobenzene sulfonamido]-pyridine) and roentgen rays.

The Wassermann reactions of the blood were repeatedly negative. The Frei reactions were repeatedly positive.

DISCUSSION

DR. F. T. BECKER, Duluth, Minn.: Dr. Robert B. Greenblatt and his co-workers had an exhibit on venereal disease at the 1940 meeting of the American Medical Association, in New York. When I discussed the subject with him, he was of the opinion that sulfanilamide and its derivatives were of only slight value for the early stages of lymphogranuloma venereum and of no value for granuloma inguinale but that they constituted the therapy of choice for chancroid.

DR. J. F. MADDEN, St. Paul: In reply to a question, the patient has not had fever therapy.

A Case for Diagnosis (Psoriasis? Lichen Planus?). Presented by DR. J. F. MADDEN, St. Paul.

M. G., a white woman aged 40, was presented before this society in December 1937, in February 1938 and in November 1938 (ARCH. DERMAT. & SYPH. **37:** 725 [April] 1938; **38:**479 [Sept.] 1938; **39:**788 [Jan.] 1939).

New lesions appear when monthly injections of 30 mg. of sodium gold thiosulfate are stopped. The patient has had thirty-eight such injections to date. This medication has effectively controlled the eruption for two years, and more intensive gold therapy clears up the eruption temporarily. However, the lesions reappear shortly after the injections are stopped.

(Histologic sections were demonstrated.)

A Case for Diagnosis (Leukaemia Cutis? Myelogenous Leukaemia?). Presented by DR. J. F. MADDEN, St. Paul.

E. T., a white woman aged 50, stated that a firm pimple appeared just within the hair line on the left side of the forehead about Aug. 1, 1940. This has grown steadily and now is an asymptomatic, slightly raised, dull red plaque about the size of a quarter-dollar. There were no other lesions found on the skin.

The white blood count varied from 35,000 to 52,000 with a preponderance of polymorphonuclear leukocytes and many immature forms of metamyelocytes, myelocytes and promyelocytes. The Wassermann reaction was negative.

DISCUSSION

DR. J. F. MADDEN, St. Paul: I do not believe that myelogenous leukaemia cutis is as rare as was formerly believed. Additional cases are recorded rather frequently. It is interesting to note that other members of the society think that specific cutaneous lesions are not extremely rare in myelogenous leukaemia.

Lichen Planus. Presented by DR. H. N. KLEIN and DR. J. F. MADDEN, St. Paul.

J. B., a man aged 73, was seen by Dr. Klein in July 1940. He stated that an eruption had appeared on the anterior surface of his legs in May 1940 and within two weeks had involved the flexor surfaces of the forearms. The lesions were papular at that time. The eruption become acute and vesicular in August, and when he was seen on September 1 he had the following types of lesions: raised verrucous violaceous papules on the anterior surface of the legs, small angular violaceous papules on the anterior surface of the legs and forearms, vesicopustules and vesicles on the legs and forearms and flat-topped white angular papules with ramifying striae on the buccal mucosa.

The Wassermann reaction was negative.

DISCUSSION

DR. STEPHAN EPSTEIN, Marshfield, Wis.: I agree with Dr. Michelson's doubts as to the diagnosis. At present the lesions on the arms and legs do not

seem to present the typical picture of lichen planus, either clinically or histologically. The lesions on the palate show some infiltration and scarring. Here, too, the picture does not correspond to what is usually seen in cases of lichen planus. The clinical lesions show definite grouping and formation of semicircles. There are bullae and remnants of them present. In view of the clinical appearance of the lesions and the fact that the patient suffers from itching, burning and paresthesias, I might consider a diagnosis of Duhring's disease.

DR. F. W. LYNCH, St. Paul: When I first saw this patient several months ago I made a diagnosis of lichen planus. There is, of course, some doubt at present, but I still think this is the correct diagnosis.

A Case for Diagnosis (Lichen Planus?). Presented by DR. J. F. MADDEN, St. Paul.

M. W., a man aged 55, stated that a painless pinhead-sized hard pimple appeared on the right side of the cheek just beyond the corner of the mouth about April 1940. The lesion grew steadily and became annular. It is now an annular lesion, 2 cm. in diameter, the center of which appears depressed but shows no evidence of scarring. The elevated annular border is about the size of the lead in a common pencil. The border is violaceous, while the central portion of the lesion is the same color as the surrounding skin. There are flat white papules with ramifying white striae on the buccal mucosa opposite the cutaneous lesion. The patient also has a large plaque of lichen chronicus simplex on the lateral surface of the left leg of nine years' duration.

The Wassermann reaction of the blood was negative.

DISCUSSION

DR. H. G. IRVINE, Minneapolis: I think that because of the induration and scalloped border of the lesion syphilis should be considered in spite of the negative Wassermann reaction.

DR. J. F. MADDEN, St. Paul: Since the use of the more sensitive serologic tests for syphilis in recent years, I have not seen an untreated patient with syphilis involving the skin and mucous membrane who did not have positive reactions to serologic tests. I think that the diagnosis of syphilis of the skin in any stage has become almost entirely a laboratory procedure.

Adenocarcinoma of the Stomach with Metastasis to the Liver; Basal Cell Epithelioma of the Forehead. Presented by DR. J. F. MADDEN, St. Paul.

A. K., a white woman aged 62, stated that there was a bleeding wound caused by an injury on the left side of the forehead in 1926. The same location on her forehead was injured again in January 1940. An open wound resulted, which did not heal. The lesion gradually spread over the scalp and down the forehead until there is now an ulcer the size of an egg. The borders are rolled, and the base is covered with crusts and a sanguineous exudate. The patient also has an adenocarcinoma of the stomach with metastasis to the liver. The Wassermann reaction of the blood was negative.

DISCUSSION

DR. J. F. MADDEN, St. Paul: This patient was shown because I thought it was unusual to see two apparently independent cancers develop in different organs in the same person.

A Case for Diagnosis (Lymphoblastoma?). Presented by DR. J. F. MADDEN, St. Paul.

E. L., a woman aged 26, was presented before this society in October 1939 (ARCH. DERMAT & SYPH. **41**:623 [Jan.] 1940). Some of the lesions have become less elevated and indurated. There may be one or two new lesions. The results of laboratory tests are the same.

DISCUSSION

DR. CARL LAYMON, Minneapolis: This condition is a most difficult one to diagnose, both clinically and histologically. After studying the sections Dr. Montgomery thought that the condition might be Kaposi's sarcoma. The continued good health of the patient over a period of several years is rather against a diagnosis of mycosis fungoides.

Pseudochancre Redux; Gumma of the Os Calcis; Syphilitic Periostitis. Presented by DR. J. F. MADDEN, St. Paul.

R. H., a Negro aged 27, stated that he was treated in 1933 with intramuscular and intravenous injections for "bad blood." He had a dime-sized ulcer on the dorsum of the prepuce about July 1939, which was treated by local caustics and healed within a month. This was accompanied by unilateral inguinal lymphadenitis, but no generalized eruption was noted. In November 1939 a Wassermann reaction of the blood was found to be positive, and he received one intravenous and one intramuscular injection of an unknown medication. The patient discontinued treatment because of financial reasons. He was admitted to the Ancker Hospital in July 1940 with an indurated, painless ulcer the size of a quarter-dollar on the dorsum of the prepuce at the site of the previous lesion. There was no lymphadenitis. The patient also had a draining sinus on the lateral surface of the right ankle, which had appeared about July 1, 1940.

Wassermann reactions of the blood were repeatedly negative. Flocculation reactions were repeatedly positive. Dark field examination was thought to show Spirochaeta pallida on one occasion, but the results were negative on many other occasions. Roentgenograms showed periostitis of the lower third of the right fibula and probable gumma of the os calcis. A roentgenogram of the chest was normal.

The patient received approximately eight intravenous injections of neoarsphenamine (average dose 0.6 Gm.), nine intravenous injections of old arsphenamine (average dose 0.45 Gm.) and eighteen intramuscular injections of 1 cc. of bismuth subsalicylate in oil during August and September 1940. The lesions are slowly undergoing involution.

Darier's Disease (Mother and Four Daughters). Presented by DR. J. F. MADDEN, St. Paul.

R. V. C. N., a white woman aged 50, stated that an eruption appeared on her face, neck, backs of the hands, forearms and shins when she was 12 years old. The eruption became more pronounced until she reached the age of about 20 and then remained stationary for several years. It has been slowly receding during the past five years. The lesions are rough, dry, scaly, follicular, keratotic papules, some of which coalesce to form plaques. The patient has two brothers and two sons who do not have the disease and four daughters who have the disease in varying degrees. The eruption is more severe in the older daughters, aged 24 and 22, than in the younger ones, aged 18 and 13. In each instance the lesions first appeared on the face, legs and backs of hands between the ages of 9 and 12 years.

A Case for Diagnosis (Atrophic Syphilitic Glossitis? Carcinoma of the Tongue? Leukoplakia?). Presented by DR. J. F. MADDEN, St. Paul.

A. B., a white man aged 62, complained of soreness and swelling on the left side of the tongue, difficulty in swallowing and swelling of the neck in July 1940. He consulted his local physician, who made a diagnosis of gumma of the tongue. He was given sixteen intravenous injections of neoarsphenamine and sixteen intramuscular injections of a bismuth compound before he was seen in the Ancker Hospital on September 21. The patient had had a penile lesion in 1904, which was followed by a generalized eruption. For two years following this he was treated with mercury tablets orally. There is a crateriform, irregular ulcer

involving the middle of the posterior third of the left side of the tongue which is painful and of cartilaginous firmness. The base seems to be healing, and there is an irregular rolled border. The papillae are missing from the dorsal surface of the tongue, and it has a shiny, glazed, atrophic appearance. The anterior cervical glands are bean sized and comparatively soft. There is an irregular bean-sized patch of leukoplakia on the buccal mucous membrane opposite the junction of the canine teeth.

A roentgenogram of the chest showed fibrosis of the upper lobes of both lungs, which was evidently due to an old pulmonary tuberculosis, although there was no apparent activity. The Wassermann reaction of the blood was 4 plus.

Histologic sections were not satisfactory. Later sections showed squamous cell carcinoma grade III.

Benign Pemphigus (Hailey and Hailey) Treated with Sulfathiazole (2-Sulfanilamidothiazole). Presented by DR. F. W. LYNCH, St. Paul.

H. W., a man aged 32, has had an eruption on the shoulders and sides of the neck nearly constantly since its onset in 1934. The lesions have appeared in groups, persisting for several weeks. At times they have completely disappeared for short periods. Axillary lesions have been evident on several occasions. A laxative containing phenolphthalein has been used occasionally but without relation to the development of new lesions. No similar eruption has been noted in the immediate family.

Treatment with numerous local applications, roentgen ray therapy and ultraviolet irradiation has had little effect on the course of the eruption. Since the culture of material from an unruptured vesicle resulted in a pure growth of Staphylococcus aureus, sulfathiazole was administered from September 27 to October 7, with almost complete healing of the eruption.

The eruption has consisted of groups of vesicles which have extended peripherally to form arcuate or annular crusted lesions. At present there are only a few small areas of crusting and a number of small depigmented scars. The miscroscopic sections show the changes reported by Hailey and Hailey and other observers as characteristic of benign pemphigus.

NOTE.—A crusted eruption of a similar nature appeared in each axilla about November 1. Sulfathiazole powder was applied, with good results, but the eruption again recurred and attained its usual extent.

METROPOLITAN DERMATOLOGICAL SOCIETY

THOMAS N. GRAHAM, M.D., *President*

ROBERT R. M. MCLAUGHLIN, M.D., *Secretary*

Oct. 21, 1940

Synovial Cyst. Presented by DR. HENRY D. NILES.

K. B., a man born in the United States, was first seen on May 18, 1940, because of erythema and edema of fourteen months' duration, involving the nail fold of the right ring finger. This area was only slightly painful at times. The condition has gradually become worse. There are also dystrophy and discoloration of the nail. Four days ago the patient's finger was incised and pus was expressed. There was no history of preceding trauma.

Wet dressings of a 1:5,000 metaphen solution were applied, with improvement. At this time roentgen ray therapy was instituted. He was given twelve treatments of unfiltered roentgen rays (75 r each), following by four exposures of 75 r filtered through 3 mm. of aluminum, with little improvement. On several occasions a glairy gelatinous fluid was expressed from under the nail fold. This

usually required considerable pressure but caused no pain. On each occasion the swelling recurred. The nail fold is separated from the underlying nail, and a probe can be inserted about ½ inch (1.3 cm.).

The patient is presented for suggestions as to therapy.

DISCUSSION

DR. LESLIE P. BARKER: I believe this lesion is a synovial cyst, although the location is not typical. I suggest surgical excision, as my experience with roentgen ray theray in these cases has not been encouraging.

DR. LAIRD S. VAN DYCK: The fluid was so viscid and thick I was not sure whether it was synovial fiuid or pus caused by an organism, such as Bacillus mucosus capsulatus. A culture should be made to see if there is an infection present before surgical intervention is attempted.

DR. ANTHONY C. CIPOLLARO: I did not see this patient, but from what I have heard so far the condition is a synovial cyst. My experience has been that these lesions disappear with roentgen ray therapy. I usually administer a full erythema dose of roentgen rays (550 r) to the lesion, closely shielded, using a filter of 3 mm. of aluminum. All the synovial cysts that I have treated by this method have responded. I am surprised that in this particular case the cyst did not disappear with four treatments. I recommend that this patient receive one more treatment, employing the dose I mentioned.

DR. MAURICE J. COSTELLO: I agree with the diagnosis of synovial cyst, although I think that there is secondary pyogenic infection. Since roentgen ray therapy has not cured it, I suggest surgical treatment or electrodesiccation, as there is already permanent deformity of the finger nail.

DR. ROBERT R. M. MCLAUGHLIN: There has been so much roentgen ray therapy given that surgical intervention is not the method of choice. I agree with Dr. Costello's idea of electrodesiccation.

Lichen Planus Atrophicus. Presented by DR. MAURICE J. COSTELLO.

E. H., a girl aged 12 years, from Bellevue Hospital, states that she has had this eruption for the past nine months. It is located on the forehead, sides of the face, forearms, thighs and legs. When she was admitted to the hospital, the eruption consisted of lentil-sized to half dime-sized annular violaceous lesions.

The borders of the lesions were slightly raised and threadlike, with pale, pigmented atrophic centers. The lesions on the extremities were typical discrete pruritic lesions of lichen planus.

Treatment has consisted of intramuscular injections of 1 cc. of bismuth subsalicylate (0.1 Gm.) at weekly intervals. At this presentation the lesions have undergone almost complete involution; pigmentation and atrophy replace the aforementioned lesions.

DISCUSSION

DR. MAURICE J. COSTELLO: I presented this patient because of the relative rarity of this atrophic type of lichen planus in a child.

DR. HENRY D. NILES: This case is interesting because the occurrence of lesions on the face is unusual.

DR. ANTHONY C. CIPOLLARO: Lichen planus is uncommon in babies and children but not rare. I have a photograph of a baby only a few months of age with lichen planus.

Perivasculitis Nodularis Necroticans. Presented by DR. MAURICE J. COSTELLO.

M. L., a woman aged 36, has had an eruption on the anterior and lateral aspects of the legs for the past year. She dates the onset of the eruption to the time when she was given potassium chloride by mouth in the treatment of an asthmatic condition, which had been present for years.

There are six to eight lesions on each leg. They are slightly tender almond-sized to quarter-sized bluish red and somewhat elevated lesions. Their surface is smooth, and there has been no tendency toward ulceration.

DISCUSSION

DR. ROBERT R. M. MCLAUGHLIN: The patient has a definite personal and family background of allergy.

DR. ANTHONY C. CIPOLLARO: Clinically the lesions are those of erythema induratum of Bazin. I am aware of the fact that some histopathologists frequently report the condition as perivasculitis nodularis necroticans. I think that both are one and the same condition.

DR. MAURICE J. COSTELLO: An eruption of this type on the legs offers difficulty in arriving at a diagnosis. It has clinical features of both erythema nodosum and erythema induratum. The location, tenderness on pressure and appearance favor erythema nodosum, whereas the chronicity, recurrence and occasional ulceration unaccompanied by constitutional reaction favor erythema induratum. The condition might be called erythema nodosum perstans. Several causes have been mentioned for erythema nodosum: pyogenic foci, drugs, syphilis, tuberculosis and gonorrhea.

Bilateral Herpes Zoster. Presented by DR. MAURICE J. COSTELLO.

J. L. a man aged 64, from Bellevue Hospital, was first seen by the presenter on Aug. 30, 1940. He complained of pain in the right side of his chest. Examination revealed a typical herpes zoster of two weeks' duration on the left side of the thorax.

On September 3, four days later, he presented, in addition to the aforementioned eruption, a typical herpes zoster in the corresponding location on the right side of the chest. There were no aberrant vesicles. The eruption observed on his first visit was at this time undergoing involution, and the lesions on the right side of the chest were in the process of evolution. The Wassermann reaction of the blood was negative.

DISCUSSION

DR. THOMAS N. GRAHAM: I recall having seen 1 other patient with bilateral herpes zoster which was more extensive than this. Several intercostal nerves on either side of the body were involved. According to the history, the eruption followed the intravenous injection of arsphenamine. In the reported cases bilateral herpes zoster has been observed in a number of patients with a history of arsenical therapy.

Follicular Atrophic Lichen Planus. Presented by DR. MAURICE J. COSTELLO.

J. D., a man aged 72, from Bellevue Hospital, presents an eruption on the lateral aspect of the buttocks and thighs and on the anterolateral aspect of the legs. It consists of discrete, closely approximated follicular lesions, forming palm-sized patches. The individual lesion, which is definitely follicular, is from pink to dark red, depending on its duration. A thin area of perifollicular dull red erythema surrounds a slight shiny depressed scaly area of atrophy. The lesions on the anterior surface of the shins are papular and verrucous, suggesting amyloidosis cutis.

In the center of several of the patches are areas of lichenification due to scratching. Histologic examination showed stratified squamous epithelium. It was greatly thinned out in places. There was a diffuse infiltration of round cells confined to the upper part of the cutis. There was an increase in fibrous tissue. Amyloid was not present. Further histologic study was made by Dr. Fred Weidman, whose diagnosis was lichen planus of the atrophic follicular type. No syphilitic lesions were present.

DISCUSSION

DR. ROBERT R. M. MCLAUGHLIN: I never saw anything like this condition. Some of the lesions on the arms are flat-topped papules. I should not want to make a clinical diagnosis.

DR. LAIRD S. VAN DYCK: It is noteworthy that the lesions coalesce into large plaques with central atrophy. I do not recall having seen lichen planus of this type.

DR. ANTHONY C. CIPOLLARO: I certainly cannot make a diagnosis of follicular atrophic lichen planus in this case. However, the evidence presented by Dr. Costello to confirm this diagnosis is adequate and acceptable. I am indeed grateful to have had the opportunity of seeing this most unusual and rare manifestation of this common disease.

DR. MAURICE J. COSTELLO: In my experience this clinical picture is a new entity which must be of extremely rare occurrence, although I saw its couterpart in a woman several weeks ago. Intradermal tests with congo red were performed in several locations on the lower extremities because the pruritic lesions suggested amyloidosis cutis. The results were negative.

CLEVELAND DERMATOLOGICAL SOCIETY

H. N. COLE, M.D., *President*

C. G. LAROCCO, M.D., *Secretary*

JAMES R. DRIVER, M.D., *Reporter*

Oct. 24, 1940

A Case for Diagnosis. Presented by DR. H. G. MISKJIAN.

R. D., a youth aged 17, has a remarkably symmetric eruption, on each side of the nape of the neck. It started about two years ago in the form of a small red pimple on the left side and gradually spread. About a year later it appeared on the right side. It has been in its present condition for about a year.

On both sides of the back of the neck, about 5 cm. from the midline, there is a linear eruption, composed of small, red, raised, hard papules. They are contiguous but not confluent and appear like beads on a string. The eruption forms a curved line, more or less paraboloid on the right side. On the left side it is irregularly curved with a looplike annular lesion in the middle. There are, in addition, some stray papules around the main lesion.

The striking feature of the histologic examination was an intraepidermal cavity containing numerous threads, branched and intertwined. Under high magnification these threads showed septums resembling hyphae. In the papillary and subpapillary layer of the epidermis there was a cellular infiltration in which monocytes predominated.

Cultures on a sugar-proof medium were negative for mycotic organisms.

DISCUSSION

DR. I. L. SCHONBERG: This patient presents some of the characteristics that were described in a paper by Wise and Rein (Wise, F., and Rein, C. R.: Lichen Ruber Moniliformis: Report of Observations at Necropsy, ARCH. DERMAT. & SYPH. **38**:251-252 [Aug.] 1938). In their case the lesions were more widespread and developed over the trunk, face and extremities. They conformed to a string of pearls. In view of the fact that there are only a few lesions, it is possible to consider this diagnosis.

DR. J. A. GAMMEL: I examined the slide and noticed some very peculiar parallel bundles that I took to be hyphae without spores. The parallel arrangement is called coremia. I believe the condition is a mycotic infection, and I hope further cultures can be studied.

DR. GEORGE BINKLEY: I also saw the bundles of hyphae in the histologic section. I think it advisable to culture some of the tissue.

DR. J. A. GAMMEL: The cultures were made from a biopsy specimen but were contaminated by staphylococci. That is why I should like to make further cultures.

DR. H. N. COLE: There was an isolated lesion on the spine that seemed to show what looked like an intraepidermal pustule, something like those seen in cases of blastomycosis. I think this case deserves further study and a further report.

DR. H. G. MISKJIAN: When I removed the biopsy specimen, with a punch, on one edge I saw a small white mass and at the time did not know what it was, but now I think it must have been a tiny abscess.

Hairy Tongue. Presented by DR. HAL ELSON FREEMAN and DR. E. B. HEISEL.

L. T., a man aged 60, presented from the department of dermatology and syphilology, Cleveland City Hospital, complained of a brown hairy growth on the tongue for three years, which has been asymptomatic until the last few months when it has interfered with deglutition.

Examination reveals an approximately triangular area, extending over the dorsum of the tongue in its middle third. This area is covered by a brown, pigmented hairlike growth about ¼ inch (0.6 cm.) in length.

Cultures on Sabouraud's sugar-proof medium resulted in a luxuriant growth of a pure strain of fungus within three days. The individual organisms were approximately 10 to 12 microns in length. Some were heavily stained with methylene blue, while others were noticeably lighter. This fungus was considered to be a variety of Streptothrix.

DISCUSSION

DR. J. A. GAMMEL: I have looked at the culture—and it is impossible to identify any organisms by looking for a moment—and I believe the organism is Monilia or closely related to it. Monilia or cryptococcus are usually found in cases of this kind. I am inclined to believe the organisms are secondary invaders.

Syphilitic Gumma of the Stomach. Presented by DR. E. B. HEISEL and DR. HAL ELSON FREEMAN.

H. B., a Negro aged 33, presented from the department of dermatology and syphilology, Cleveland City Hospital, for the past eleven months has had recurrent exacerbations of epigastric distress, which were relieved by food and alkalis. He was asymptomatic between exacerbations. He stated that from Aug. 1, 1940 to the date of admission to the hospital, August 27, he had vomited after each meal and had lost 35 pounds (16 Kg.). He gave a history of a chancre in 1929 and fairly regular treatment for syphilis from 1930 to 1933. On Oct. 5, 1940 an exploratory laparotomy was performed, at which time a subtotal resection of the stomach was performed.

Grossly the resected portion of the stomach was thickened and firm. The serosa was smooth and shiny. All layers of the stomach wall could be visualized. The mucosa showed an irregular, well defined ulceration, 6 by 4 cm., with a necrotic base and a slightly rolled, nonindurated, serpiginous border.

The hemogram and the urine were normal. Serologic tests of the blood for syphilis gave strongly positive results on two occasions. The cerebrospinal fluid was normal. A gastric analysis showed retention of food given twelve hours before the analysis and achlorhydria. Two roentgenograms of the stomach showed a spastic deformity of the prepylorus with an "ulcer niche" along the lesser curvature. There was retention of 70 per cent of a barium sulfate meal six hours after administration.

Histologic examination revealed thickening of the wall of the stomach in which all three layers participated. The mucosa was edematous and hyperemic and in areas showed ulceration. The base of the ulcer was the seat of acute suppurative inflammation. Throughout all layers, especially the submucosa and muscularis, were diffuse and focal perivascular accumulations of cells, predominantly plasma cells. Small round cells, epithelioid cells and fibroblasts were also seen in the infiltrate. No giant cells were observed. Spirochaeta pallida was not found on examination of specially stained sections.

DISCUSSION

DR. GEORGE H. CURTIS: I should like to ask the presenters when the diagnosis was made, before or after operation?

DR. H. N. COLE: I should also like to ask whether the surgeons inquired as to the desirability of operation or of possible further antisyphilitic therapy before going ahead with the operation.

DR. HAL ELSON FREEMAN: The diagnosis was not made preoperatively. The patient was known to have positive reactions to serologic tests, but it was felt that he had a peptic ulcer or carcinoma. That is the reason he was subjected to operation. The surgeons did not inquire specifically as to whether therapy should be given before this was undertaken, but I must admit that if they had I should have agreed with the diagnosis of latent tertiary syphilis and peptic ulcer. Histologically after operation the lesion was seen to be a perivascular plasma cell infiltrate, which is characteristic of syphilis.

DR. H. N. COLE: This type of case certainly is rare.

DR. NEWTON KRUMDIECK (by invitation), New York: I should be interested to see a number of sections, because often syphilis of the stomach turns out to be scirrhous carcinoma. I do not believe that the perivascular plasma cell infiltrate would necessarily prove the lesion to be syphilis.

DR. H. N. COLE: It seems to me that the histologic evidence in a case of late syphilis places the burden of proof on those who say the condition is not syphilis.

Varicose Ulcer of the Leg in a Youth. Presented by DR. HAL ELSON FREEMAN.

R. G., a boy aged 15, presented from the department of dermatology and syphilology, Cleveland City Hospital, complained of a chronic ulcer of the left leg.

Examination shows hyperpigmentation of an oval, slightly irregular area, approximately 6.5 by 9 cm. in size, on the anterior surface of the lower third of the left leg.

When the boy was first seen on Nov. 8, 1939, a history was obtained that the ulceration had been present for four years, in spite of various treatments, and that tests of the blood had given negative results and roentgenograms of the chest had been normal.

Four dime-sized to silver dollar–sized deep "punched-out" ulcers with necrotic bases and tenderness on pressure were present. Veins as large in diameter as a fountain pen were palpable and visible in the leg and thigh when the proximal end of the thigh was compressed.

Serologic tests of the blood for syphilis gave negative results. The hemogram was normal, and no sickling of the erythrocytes was observed.

Treatment by injection of autogenous blood under the ulcers, cross stripping with adhesive tape, ultraviolet irradiation and the application of Aloe vera leaf and Aloe vera ointment resulted in temporary benefit. By March 1940 there was further benefit apparent, following injection into the veins of a solution of sodium morrhuate. Activity recurred, however, apparently due to recanalization of these veins.

On Sept. 28, 1940 the left great saphenous vein was ligated. In less than two weeks the ulcers were practically healed, after the local application of Aloe vera leaf.

DISCUSSION

DR. E. W. NETHERTON: I previously saw this patient on three occasions, and I thought he might have sickle cell anemia but was unable to prove it. There was decided edema of the legs because he was ambulatory, and he would have some varicosities of the veins, but at no time did he have eczema or dermatitis around the ulcers. They were clearcut ulcers without dermatitis. It is extremely unusual to see this type of ulcer in a child.

Squamous Cell Epithelioma of the Mouth with Invasion of the Base of the Skull. Presented by DR. GEORGE M. STROUD III.

J. K., a man aged 63, presented from the department of dermatology and syphilology, the University Hospitals, was seen in June 1939 because of an indurated ulcerated lesion of the left upper alveolar ridge of three months' duration. Histologic examination revealed the lesion to be a well differentiated squamous cell epithelioma.

After extraction of several remaining teeth the lesion was treated by interstitial irradiation with radium needles of low intensity, a total dose of 2,121 milligram hours being given. The reaction healed within four months, only to be followed three months later by ptosis of the left upper eyelid, paresthesia over the ophthalmic division of the left trigeminal nerve and severe headache. A firm enlarged lymph node developed beneath the angle of the right side of the jaw at the same time.

Roentgenograms made in March 1940 showed a mass in the posterior two thirds of the right middle cranial fossa and bone destruction in a similar area on the left side. Examination revealed no abnormality in the nasopharynx.

Treatment, starting on April 11 and continuing through twenty consecutive week days, consisted of giving 2,500 r to the intracranial tumor and 3,000 r to the lymph node at the angle of the right mandible.

The patient's frontal headache vanished; the mass inside the skull became slightly smaller, and the lymph node was barely palpable when he was examined on October 16. On this date there was total blindness of the left eye with atrophy of the optic nerve and incipient cataract. In addition there were left internal and external ophthalmoplegia, anesthesia of the left cornea and hypesthesia of the supraorbital region, representing involvement of the second, third, fourth, fifth and sixth cranial nerves. A peculiar, fairly soft mass, 3 by 3 by 5 cm., was present in the region of the posterosuperior part of the right sternocleidomastoid muscle. Just below this and in an analogous region on the opposite side of the neck were several small hard lymph nodes.

DISCUSSION

DR. H. N. COLE: This case is the first one that my associates and I have encountered in which an extension to the brain has occurred from epithelioma of the mouth.

Dermatomyositis. Presented by DR. E. W. NETHERTON and DR. GEORGE H. CURTIS.

C. L., a woman aged 48, has been in poor health for the past four or five years. Her symptoms have been in the main related to the gastrointestinal tract. She has been constipated for years and has suffered from periodic attacks of pernicious vomiting. She has been treated for colitis and spastic colon and has submitted to two hemorrhoidectomies during the past sixteen years. For the past two years she has noticed a progressive muscular pain, tenderness and weakness and has lost 20 pounds (9 Kg.).

In January 1940 a pruritic red scaly plaque developed just below the left breast. The plaque enlarged, and other plaques appeared on the right side of the trunk. The eruption ultimately became a diffuse erythroderma, sparing only the palms, soles and dorsa of the hands. On the face and neck there have been a few transient squamous lesions.

There have been three almost complete remissions of the eruption during the past year. Recurrences or exacerbations, which have occurred without any apparent reasons, have consistently been initiated by edema and redness of the skin. The edema has always been most intense on the lower extremities. The muscular pain and tenderness were most severe in the legs, but the muscular weakness has always been most apparent in the upper extremities. For the past few weeks dysphagia has been a prominent symptom.

At present the cutaneous manifestations are not so conspicuous. The edema and erythema have subsided greatly. There is a mild diffuse erythroderma, involving the trunk and all the extremities. There is a sharply demarcated margin of the eruption on the wrists and the lateral and dorsal surfaces of the feet. There is depigmentation on the arms in the areas involved by the erythroderma. This is accompanied by patchy hyperpigmentation on the dorsa of the hands and the sides of the face and neck.

The subcutaneous fat has almost disappeared from the upper portion of the chest and in the supraclavicular regions. Absorption of the subcutaneous fat and atrophy of the facial muscles have produced a fixed or expressionless facies.

The tongue is red, and there is some atrophy of the filiform papillae. Atrophy of the muscles of the arms and shoulder girdle is apparent, but muscular tenderness is not a prominent symptom. There is relaxation of the anal sphincter because of muscular weakness. The patient cannot walk without assistance.

The temperature has ranged from 99.6 to 97.6 F. There were 3,920,000 erythrocytes, 4,400 leukocytes and 77 per cent hemoglobin. The differential count showed 71 per cent neutrophils, 6 per cent eosinophils, 16 per cent lymphocytes and 7 per cent monocytes.

Serologic tests of the blood for syphilis gave negative results.

Urinary excretion of creatine ranged from 97 to 596 mg. in twenty-four hours. The total serum proteins amounted to 5.7 Gm., with 3.1 Gm. of albumin and 2.6 Gm. of globulin. The sternal puncture showed normal results. The cerebrospinal fluid was normal.

Tissue was removed from the skin of the leg and also from the gastrocnemius muscle for histologic examination. The epidermis showed several layers of hyperkeratosis with some parakeratosis. There was mild acanthosis. There was some intracellular and intercellular edema in the malpighian layer. The basal cell layer was intact. The corium showed edema in the papillary and the superpapillary areas. There was some edema deeper in the corium. This was accompanied by vascular dilatation and a mild perivascular infiltration. The infiltration consisted mainly of small lymphocytes, fibroblasts and occasional polymorphonuclear eosinophils. There was an occasional plasma cell.

The muscle showed variation in the size of the fibers. There was also a separation of the fibers. There was slight edema with an obliteration of the transverse markings of the muscle fibers. Some fibers showed a basophilic, granular degeneration. In places there was a multiplication of the muscle nuclei arranged in rows along the axis of the fibers. There was also an interstitial inflammatory reaction with dilatation of the small blood vessels and an infiltration of small lymphocytes and an occasional eosinophil and fibroblast.

Treatment has consisted of administration of large amounts of vitamin B complex by mouth and of mass of ferrous carbonate, blood transfusions and artificial fever therapy produced by typhoid protein shock. She has also taken aminoacetic acid, 1 drachm (4 cc.), three times a day. Topical applications have consisted of boric acid ointment and olive oil. Improvement did not occur until after the fever therapy was instituted.

DISCUSSION

DR. J. E. FISHER: I should like to ask the presenters what type of treatment was used, especially the method of typhoid therapy.

DR. H. J. PARKHURST, Toledo, Ohio: The scleroderma-like thickening which is often observed with this condition I found on the abdomen, although it was absent on the extremities. I did not find the degree of pigmentation which I have seen in other cases of this condition.

DR. BENJAMIN LEVINE: It seemed to me that the pruritus was out of proportion to what is usually seen in this type of case.

DR. E. W. NETHERTON: Any one who is interested in looking up the clinical manifestation of this condition should consult the recent article by O'Leary and Waisman (O'Leary, P. A., and Waisman, M.: Dermatomyositis: A Study of Forty Cases, ARCH. DERMAT. & SYPH. **41**:1001-1019 [June] 1940). They emphasized the fact that the condition is primarily a polymyositis and stated the belief that the change occurs in the muscles and that there are cases in which the myositis occurs without the cutaneous manifestation, just as pellagrous avitaminosis occurs without manifestation of pellagra. It is striking that this patient's primary symptoms were related to the muscles. She had had generalized myositis with pain and weakness coming on, and the cutaneous eruption appeared later. The muscles most frequently involved are the shoulder girdles and the upper extremities, most strikingly demonstrated in our case. Fever is not always present. The symptoms may be acute or chronic. The symptoms are out of all proportion to what one finds in the muscles. This case also is interesting because of the large urinary excretion of creatine. O'Leary and Waisman found this result in a certain number of their cases. When the patient has a relapse, the skin becomes very red and edema is striking. There is no cardiac or nephritic basis for it and the blood and proteins are normal, so it must be related to the general systemic condition. Studies were made to rule out Addison's disease. These show that he does not have hypoadrenal function. I do not believe too much importance should be placed on the presence or absence of pruritus.

Pyoderma Faciale. Presented by DR. H. N. COLE and DR. JAMES R. DRIVER.

F. W. I., a woman aged 31, has been married for six months and is four months pregnant. In February 1940 she noticed a red, raised spot on the left cheek, and soon all of her face became involved. The condition has not been pruritic. She has noticed many small spots filled with pus which have developed over her face.

Over the entire face, with the exception of the lower eyelids and near the hair line, there is a dark red erythema. Superimposed on it are numerous tiny pustules. The borders of the lesions are fairly sharply marginated and slightly raised, with adjacent normal skin. There are a few acneform lesions over the upper part of the sternum. The skin otherwise is entirely clear.

Histologic examination showed an epidermis with some intercellular and intracellular edema. The papillary portion of the corium showed large numbers of dilated capillaries and/or lymph spaces, about which were moderately dense infiltrations of a polymorphous type with a number of plasma cells. The subpapillary corium showed a slight infiltrate. There was no significant fibroblastic proliferation. Two sebaceous glands were visible and one seemed to be fairly normal. The other showed a dense, cellular infiltration of polymorphous type. The sweat glands seemed somewhat larger than normal. The picture was that of subacute inflammation with extensive vascularization of the papillary and subpapillary layers of the cutis and of the sebaceous glands with a cellular infiltrate.

Therapy has consisted of one treatment with filtered roentgen rays, application of a sulfur lotion and ingestion of yeast tablets.

DISCUSSION

DR. H. J. PARKHURST, Toledo, Ohio: I cannot accept this case as one of pyoderma faciale. I have had some patients with this condition in my practice, and, as O'Leary and Kierland have described (O'Leary, P. A., and Kierland, R. R.: Pyoderma Faciale, ARCH. DERMAT. & SYPH. **41**:451-462 [March] 1940), the disease is characterized by deep, undermined pustules and cystlike lesions. The lesions in this case are not of that type and are accompanied by considerable erythema. I thought the condition was a severe rosacea or perhaps rosacea-like tuberculid of Lewandowski.

DR. HUGO HECHT: I think this condition is a Demodex infection. I have seen patients with this condition, and the picture is the same as that presented by this patient and similar to acne or rosacea.

DR. HAL ELSON FREEMAN: I agree with the diagnosis of pyoderma faciale and suggest therapy with sulfathiazole (2-sulfanilamidothiazole).

DR. H. G. MISKJIAN: Since Dr. Hecht has called attention to Demodex, I think I should say a few words in regard to this question, which interests me greatly. The eruption impressed me as an intense example of rosacea. I have for some time past reached the conclusion that the condition called rosacea is nothing but the result of Demodex infestation. A young woman came to me two or three years ago with a large inflammatory patch on the left cheek. It was raised, red and infiltrated. It looked like rosacea, but I did not feel justified in making a diagnosis of unilateral rosacea. To make sure that it was not tuberculosis, I performed a biopsy, which showed only an inflammatory process. Repeated irradiation with large doses gave no definite result. Some time later I saw another patient with a condition similar to that of the first one. It then occurred to me that since the lesion was unilateral, it must be due to a local cause. I looked for Demodex and was surprised to find it. The persistent use of an ointment containing 10 per cent sulfur and 5 per cent peruvian balsam completely cleared up the patient's eruption within two months. I asked my first patient to return and prescribed for her the same treatment. She improved rapidly and was cured in about three months. In her case, however, the eruption left a certain degree of pitting because of the long duration of the disease.

Since that time I have made it a rule to look for Demodex in all eruptions of rosacea or that look like rosacea. I have found these organisms almost always, and treatment with sulfur ointment has been uniformly successful. I had a case in which the lesions were particularly extensive, similar to those the patient presented today. The patient, a woman, had been given irradiation and injections of a gold compound, with no result. I saw her in April and prescribed sulfur ointment. By the end of August she was well.

I am inclined to ascribe the improvement noticed in the case under discussion to the sulfur lotion rather than to the irradiation. I think sulfur ointment is more efficient than the lotion because it can be rubbed into the pores. It sometimes proves irritating, particularly if it contains peruvian balsam. For this reason I ask my patients to discontinue its use for two days after they have used it for three consecutive nights.

DR. H. J. PARKHURST, Toledo, Ohio: I have also observed numerous cases in which rosacea has cleared up with the use of a sulfur lotion. This result upholds the Demodex theory, but I do not see how it can explain the case of rosacea keratitis.

DR. E. W. NETHERTON: In my experience the Demodex is easily found in some cases and difficult or impossible to find in others. I should like to ask Dr. Miskjian if he thinks that in all cases of rosacea the condition is due to Demodex and if not in what type of case the Demodex should be present.

DR. H. G. MISKJIAN: It has been said and it is still stated in most textbooks that Demodex is found on normal skins. I am not prepared to say that this is not true, but in a few control cases of ordinary acne and of comedos I have not found it. I find it easily in cases of rosacea. I never use sulfur therapy unless I find Demodex. One should look for the organism in the primary element, which is characteristic: a small red conical papule, about 1 mm. in diameter, with a tiny drop of white, turbid fluid at its top.

DR. EUGENE ARDAY, Lakewood, Ohio: Dr. N. P. Anderson, in California, and I have been investigating this question, and every time we see each other we check on our observations. Demodex cannot be on normal skin according to my observations, and is found only in cases of rosacea according to the observations of Anderson. Another thing that is interesting is that I have had some cases in which severe dermatitis developed from sulfur therapy. In these I have had success with pyrethrum ointment. It should be stated, however, that all patients with rosacea do not get well with sulfur or pyrethrum therapy.

DR. GEORGE H. CURTIS: I should like to ask Dr. Miskjian if he has found Demodex in pustules on the cheeks. I have been able to find them on the nose but not on the cheeks.

DR. H. G. MISKJIAN: I usually take all my specimens from the cheeks and forehead. It is harder to find them on the nose. I do not contend that in all cases of rosacea the condition is caused by Demodex.

DR. H. N. COLE: Although this patient has been under treatment only a short time, there has been decided improvement. The indurated character of the lesions has disappeared to a large degree and the classic picture of the disease is not so apparent. This patient resembles closely the one Dr. Driver and I presented at the May 1940 meeting of this society (ARCH. DERMAT. & SYPH. **43**:572 [March] 1941).

Granuloma Inguinale. Presented by DR. JAMES E. ENGELER and DR. HAL ELSON FREEMAN.

M. E. B., a Negress aged 21, presented from the department of dermatology and syphilology, Cleveland City Hospital, complained of sores on the genitalia, which began in February 1940 as small pimples which gradually spread. In March 1940 a physician was consulted, and he gave her white pills to be taken by mouth and a "yellow medicine" which was injected into a vein of the arm twice a week for four weeks and once a week for twelve weeks. There was no improvement, and the patient was referred to Cleveland City Hospital.

The urine and the hemogram were normal. The reaction to a formaldehyde ("formol-gel") test was strongly positive. The serologic tests of the blood for syphilis gave negative results on three occasions. Dark field examinations revealed no spirochetes. A smear made from tissue curetted from the lesion showed several large mononuclear cells which contained encysted small bipolar bodies in their cytoplasm. The Ito-Reenstierna reaction was negative. The Frei test showed a 1 to 2 plus reaction.

The results of physical examination were essentially normal except for changes on the external genitalia. The prepuce and labia minora are indurated and enlarged. The prepuce measures about 5 cm. in its long axis. On the external surfaces of the labia minora there are several granulomatous rounded lesions with clean, beefy red bases. On the left side of the prepuce near its base there is an elevated tumor with rolled edges. The epithelium is intact over this lesion but is interrupted at the junction with the other lesions. The inguinal nodes are small and nontender.

Histologic examination of tissue from the ulcer showed absence of epithelium at the end of the section. The epithelium was atrophic, and there were several, long, thin downward epithelial projections into the corium. In the upper part of the corium there was a dense infiltrate, consisting principally of plasma cells, lymphocytes, fibroblasts and fibrocytes, numerous polymorphonuclear leukocytes and an occasional large mononuclear cell with an eccentrically placed nucleus. Many newly formed capillaries were seen.

Histologic examination of a lymph node from the right inguinal region showed an intact capsule. Broad inflammatory bands were seen extending from beneath the capsule toward the center. This inflammatory process was composed of numerous newly formed blood vessels, fibroblasts, plasma cells, small round cells and red blood cells. Throughout the substance of the node there were several large focal accumulations of moderately sized lightly stained mononuclear cells, which showed a reticular cytoplasm and were presumed to be reticulum cells. Examination of the remaining portion of the node revealed normal architecture.

Treatment has consisted of three intramusclar injections of fuadin, a total of 6 cc.

Granuloma Inguinale. Presented by DR. E. B. HEISEL and DR. HAL ELSON FREEMAN.

W. N., a Negro aged 26, presented from the department of dermatology and syphilology, Cleveland City Hospital, complained of an ulcer on the perineum for six months. He stated that the lesion began as a small "pimple" and attained its present size within three weeks. He gave no history of genital lesions or of a urethral discharge.

On the perineum, extending from the base of the scrotum to the anus, there is an irregular, sharply defined deep ulceration, 4 to 6 cm. in width. The ulcer has a beefy red base with a piled-up, nodular, indurated border. The induration extends about 1 cm. beyond the edge of the ulcer. Near the anus the tissue is piled up into several tumor masses, 1 to 2 cm. in diameter and 1 to 1.5 cm. in height. No perirectal lymph nodes are palpable. The inguinal lymph nodes are moderately enlarged bilaterally and are discrete, firm, and nontender. The patient presents no clinical manifestations of syphilis.

The hemogram and the urine were normal. The serologic tests of the blood showed a moderately positive reaction to a Kline test and a negative Wassermann reaction on four occasions. Examination of the cerebrospinal fluid revealed 4 cells per cubic millimeter, a weakly positive reaction to a Pandy test, a high first zone curve to a gum mastic test and a moderately positive Wassermann reaction. Tissue smears stained by Giemsa's method revealed the presence of Donovan bodies. The reaction to a formaldehyde ("formol-gel") test was positive. The Frei test gave a negative result, as did the Ito-Reenstierna test.

Histologic examination of tissue from the edge of the ulceration revealed acanthosis and spongiosis in the epidermis. Dense focal accumulations of infiltrating cells were found throughout the corium and extending into the hypoderm. These consisted predominantly of plasma cells. Epithelioid cells, neutrophils, small round cells, fibroblasts and newly formed blood vessels were also seen. In the denuded area the deeper portions of the remnants of the epithelial pegs presented a marked degree of spongiosis, but no mitotic figures were observed.

Treatment has consisted of intramuscular injections of fuadin over a period of two weeks.

DISCUSSION ON CASES OF GRANULOMA INGUINALE

DR. GEORGE H. CURTIS: I should like to ask if it is the opinion of any of the members that a fetus could be infected with granuloma inguinale in passing through the birth canal?

DR. H. N. COLE: I do not know of any such case in my experience in Cleveland, and I am not acquainted with any in the literature. However, I do not see why it would not be possible for a woman with lymphogranuloma venereum or granuloma inguinale to infect the fetus when it passes through the birth canal, just as it is possible for a physician to contract these diseases from handling such a patient. I think the case of the woman is interesting because of the decided edema and hypertrophy present. It is known that this picture, usually called esthiomene, is seen in lymphogranuloma venereum, but here it is in a case of granuloma inguinale. Therefore, it is not a specific reaction.

DR. HAL ELSON FREEMAN: A lymph node was removed from the inguinal region of the woman patient, and it showed chronic granulomatous inflammation. Many plasma cells were present. It was interpreted as showing changes due to granuloma inguinale.

Nodular Cutaneous Eruption Associated with Malignant Lymphoblastoma.
Presented by DR. OTTO E. L. SCHMIDT.

J. M., a man aged 49, presented from the department of dermatology and syphilology, the University Hospitals, complained of a nodular eruption of the left thigh for three and one-half months. Two years ago he began to suffer loss of weight and strength and pyuria. One year ago he entered the hospital because of ascites, loss of weight and dyspnea. Histologic examination of an axillary node revealed malignant lymphoblastoma. A course of roentgenotherapy reduced the generalized lymphadenopathy. Seven months ago he reentered the hospital with erysipelas, recurrent cervical and axillary lymphadenopathy and splenic and hepatic enlargement. A roentgenogram of the chest revealed no enlarged mediastinal nodes. Three and one-half months ago he noted a cluster of purplish red firm cutaneous nodules, 1 to 1.5 cm. in diameter on the upper anterior portion of the left thigh in an area 10 by 20 cm. The inguinal and axillary nodes were enlarged.

Examination showed enlarged cervical, axillary, epitrochlear and inguinal nodes. The chest was clear. The liver was enlarged a handbreadth below the costal margin. The spleen was palpated 3 fingerbreadths below the costal margin.

Above and along the left inguinal fold are numerous discrete nontender small reddish nodules. One nodule is present in the right pubic region, and one deep nodule is in the anterior middle region of the left thigh.

The hemogram has always been normal. Urinalysis revealed considerable albumin and many white blood cells. Cystoscopic examination revealed a tumor mass in the region of the trigon.

Histologic examination of a nodule revealed chronic granulomatous inflammation of the skin.

A course of roentgenotherapy consisting of 800 r, given from July 30 to October 1, caused complete involution of the nodular eruption.

BRONX DERMATOLOGICAL SOCIETY

LEO SPIEGEL, M.D. *President*

HENRY SILVER, M.D., *Secretary*

Oct. 24, 1940

Mycosis Fungoides D'Emblée. Presented by DR. CHARLES WOLF.

F. M., aged 55, a mother of 4 children, has had no serious illness in the past. She has had no miscarriages. The husband is living and well.

A lesion appeared on her chin about three months ago. On first appearance it was no larger than a millet seed. It has grown to the present size in the past three weeks.

Physical examination revealed a healthy-appearing person except for the presence of the tumor on the chin. There was no regional adenopathy and no palpable enlargement of the spleen and liver.

On the left side of the chin there is a reddish, round and rather firm tumor, the size of a hazelnut. There are no enlarged submental glands. The Wassermann reaction was negative.

The histologic diagnosis reported by Drs. Klemperer, Otani and Peck was mycosis fungoides.

DISCUSSION

DR. SAMUEL M. PECK: Solitary lesions of mycosis fungoides have been reported, but the occurrence is rare. Histologically the lesion is lymphoblastoma.

DR. DAVID L. SATENSTEIN: To make a clinical diagnosis of mycosis fungoides d'emblée on the basis of this solitary lesion is extremely difficult. I should rather consider sarcoma or possibly lymphatic leukemia. In conditions of this kind that fall into the tumor class the central portion of the lesion usually breaks down, resulting in ulceration. The histologic description would still leave one in doubt as to whether the lesion is one of mycosis fungoides unless it shows the picture of polymorphous infiltration. The diagnosis is still questionable.

I recall a case of this type in a boy aged 14 or 15 years with an isolated lesion on the chin. A diagnosis of possible sarcoma was made. The tissue showed leukemia. The boy died in two years from generalized sarcoma. It is possible that the case presented may fall into the same category. In view of that I should make this diagnosis provisionally. If the mycosis fungoides is associated with mitotic figures, radiotherapy will be of benefit; the lesion should respond to irradiation rapidly.

DR. ADOLPH ROSTENBERG: I should hesitate to make a diagnosis of mycosis fungoides on the basis of this solitary tumor, even in the presence of the suggestive microscopic report, since in lymphoblastoma the microscopic picture often

changes from time to time. In a patient under my observation a solitary tumor diagnosed as lymphosarcoma developed. The lesion yielded promptly to roentgen treatment but recurred repeatedly. The blood picture was entirely normal. After a few years, however, the lymphatic glands became enlarged and the blood showed an unmistakable picture of lymphatic leukemia, confirmed at autopsy. I should therefore withhold a definite diagnosis in this case, except for labeling it one of lymphoblastoma, and watch for further developments.

DR. CHARLES WOLF: I agree with Dr. Satenstein that the diagnosis on clinical grounds is difficult. In fact, the possible diagnoses are sarcoid, epithelioma and lymphosarcoma. There are no clues to help one in the diagnosis. Since the biopsy specimen was taken the lesion has doubled in size. It might be that other lesions may develop shortly. With regard to radiotherapy, the response would be effectual whether the lesion is leukemia, lymphosarcoma or mycosis fungoides. One dose would melt such a lesion in a short time but would not prevent other tumors from appearing at a later date.

Lichen Planus Spinulosus et Atrophicus. Presented by DR. PAUL GROSS.

A. M., a housewife aged 58, was presented before the Section of Dermatology and Syphilis, New York Academy of Medicine in October 1940 (ARCH. DERMAT. & SYPH., this issue, p. 727).

Since the presentation the patient has received treatment with nicotinic acid, 75 to 150 mg. per day. The itching has subsided, but there is no change in the clinical picture.

DISCUSSION

DR. SAMUEL M. PECK: The histologic picture seems typical for lichen planus. In the presence of lichen planus one should consider etiologic factors, such as heavy metals or even fungi.

DR. SAMUEL FELDMAN: This case is identical with the cases of a variation of lichen planus which I have described (Feldman, S.: Lichen Planus et Acuminatus Atrophicans, ARCH. DERMAT. & SYPH. **5**:102-113 [Jan.] 1922). Graham Little described this syndrome originally as lichen spinulosus et folliculitis decalvans. These lesions, however, are not of the spinulosus type but show perifollicular round cell infiltration with an increased granular layer typical of lichen planus around the hair follicle. The condition, therefore, is entirely different from lichen spinulosus.

It is noteworthy that the atrophy usually affects the scalp. I have seen atrophy in this disease occurring elsewhere on the body, but the head is the most commonly involved. This is the reason for the title used by Graham Little, which of course is a misnomer. The loss of hair in this patient is not due to scars following pustules but to real atrophy, as is sometimes seen in patients with lichen planus.

DR. DAVID L. SATENSTEIN: I did not see atrophy or scars in this patient. The atrophy that occurs in cases of this kind is due to pressure on the follicle which causes the loss of hair. Lichen planus around the hair follicle is rare, and I have seen but few examples.

DR. PAUL GROSS: The interesting feature in this case is the fact that the patient first had lichen planus without any signs of lichen spinulosus and now presents lichen spinulosus without any clinical evidence of lichen planus. The absence of lichen planus though is only clinical, since the histologic section of a typical lesion of lichen spinulosus shows in a small area near the follicular orifice all the epidermal and dermal changes characteristic of lichen planus, as described by Dr. Feldman. I agree with Dr. Satenstein that there is no atrophy of the affected areas of the scalp except that around the hair follicles, which is apparently due to the short duration of the disease.

A Case for Diagnosis (Cheilitis?). Presented by DR. LOUIS CHARGIN.

Miss C. B., aged 38, has suffered from an eruption of the lower lip for the past three years. It appeared first after a sunburn. The process affects mainly

the lower lip, but not in its entirety. The outline of the eruption is somewhat irregular and for the most part limited to the mucocutaneous surface. There is some involvement of the mucous surface. There are redness, scaling and slight fissuring. The upper lip shows merely scaling. There is considerable pain. A variety of local remedies, vitamin B complex and light-protective ointments have been tried without benefit. The process gets better spontaneously or as a result of therapy but does not disappear entirely.

DISCUSSION

DR. SAMUEL FELDMAN: The condition in this case appears to be cheilitis of the glandular type. The involvement is rather deep; there is definite infiltration present. I have had good results with roentgen ray treatment and suggest that it be tried.

DR. ADOLPH ROSTENBERG: If the condition is cheilitis exfoliativa I suggest thorough electrodesiccation. This therapy was successful in cases of this kind when other methods failed.

DR. PAUL GROSS: The patient should be impressed with the importance of a biopsy. If lupus erythematosus can be ruled out, actinic cheilitis should be considered, especially in view of its role as a precancerous condition (Ayres, S.: Chronic Actinic Cheilitis, *J. A. M. A.* **81**: 1183 [Oct. 6] 1923). I see no evidence of cheilitis glandularis.

DR. MARION B. SULZBERGER: The appearance of the condition and the course speak in favor of lupus erythematosus. I agree it is not cheilitis glandularis.

It has been my experience that lupus erythematosus affecting the lips is refractory to all forms of treatment; it acts in this respect like lichen planus of the mucous membranes. In cases of this kind I have administered large doses of gold and bismuth compounds not only in the usual way but also a bismuth compound by mouth. Moreover, I have administered sulfanilamide and its derivatives without effect, and various vitamins, recently recommended, have also proved of no avail. I think, however, that the new forms of oral bismuth medication are worth trying in cases of lichen planus and lupus erythematosus, particularly when the lesions are confined to the mucous membranes of the lips.

DR. SAMUEL M. PECK: The patient's condition must be differentiated from dermatitis of the lip due to sensitivity from lipstick, for instance. It is unusual to see the absence of a slight extension of the process immediately around the lip in cases of dermatis venenata.

The diagnosis seems to me to be lupus erythematosus. Ordinarily I suggest germanin as the medicament of choice, because lupus erythematosus of the lips is notoriously resistant to treatment. My experience with the use of germanin has been particularly gratifying in cases in which there is involvement of the mucous membranes.

DR. LOUIS CHARGIN: I appreciate the suggestions offered. Naturally, I thought of lupus erythematosus. I have seen many examples of lupus erythematosus of the lips, and I am not willing to make this diagnosis in this case.

Unfortunately, the patient will not submit to a biopsy. My experience has been similar to that of Dr. Sulzberger. It is difficult to treat successfully patients with this condition, but in the course of years the process will probably disappear. Electrodesiccation, in my opinion, is the method of therapy least likely to yield good results. I was unable to trace the condition in this patient to any contact. The patient does not use lipstick.

Lichen Nitidus. Presented by DR. SAMUEL PECK and DR. ABNER KURTIN (by invitation).

A. K., a physician aged 29, presents an eruption which first appeared about six years ago in the form of small papules on the volar surfaces of the wrists. In the next six years and up to the present there has been a gradual increase of the eruption. At present the condition involves the arms, genitocrural regions and penis. There are no subjective symptoms.

The characteristic lesion is a small papule the color of the skin showing a shiny surface. For the most part these papules remain isolated, but some show a tendency to coalesce. On the elbows there are lesions forming a scaly patch, and in this location there is some resemblance to psoriasis. There has been no involution of any of the lesions. The lesions are not noticeable when the skin is tanned by the sun. There is no evidence of tuberculosis after years of careful observation. The reaction to a tuberculin test with a dilution of 1:10,000 was slightly positive.

No therapy has been attempted.

The histologic study of the excised tissue showed the typical structure of lichen nitidus.

DISCUSSION

DR. DAVID L. SATENSTEIN: I wish to refer to an article (Ellis, F. A., and Hill, W. F.: Is Lichen Nitidus a Variey of Lichen Planus? ARCH. DERMAT. & SYPH. **38**:569-573 [Oct.] 1938) in which the authors claimed that lichen nitidus is a form of lichen planus, with which I do not agree. Exactly where lichen nitidus belongs I do not know. Whether therapy has any value I cannot state. In my experience therapy aggravates the condition.

I have given roentgen therapy, 2,000 r in a course of six weeks, but have seen no response. I also tried minute doses of tuberculin, giving a large number of injections, without benefit.

DR. CHARLES WOLF: Since therapy has not yet been employed, I suggest that a fairly large patch be exposed to roentgen rays and that 1,000 r be given over a period of two months in divided doses, about 150 r per dose.

DR. SAMUEL M. PECK: This case is of interest because the patient is a physician. Some of the most important observations of disease processes have been self observations of medical men. It can safely be stated that the cause of lichen nitidus is unknown. In spite of the histologic picture few will agree that there is any relation to tuberculosis. Judging from the distribution of the lesions, the toxins or noxa reach the skin hematogenously.

Pityriasis Rubra Pilaris. Presented by DR. PAUL GROSS.

R. L., a white man aged 39, states that a generalized eruption appeared thirteen years ago following an operation for hernia. Since that time the condition has persisted. A few months ago the patient was hospitalized for eighteen days on account of a second operation for hernia. He claims that during that period the eruption showed considerable improvement.

There is a diffuse, erythematous and scaly eruption of the scalp, particularly pronounced at the frontal hair line. The eyelids, the region of the mustache and the ears are also erythematous and scaly. On the chest and the extensor surfaces of the upper extremities are irregular patches resembling psoriasis. In addition, there is a widespread eruption of papules with a central follicular hyperkeratosis or actual follicular plugging. These lesions are numerous, confluent and yellowish pink and have a grater-like feel. On the shoulders they form large plaques. The follicular plugs are pronounced on the dorsa of the hands and proximal phalanges of the fingers. There is diffuse hyperkeratosis of the palms and soles. Especially on the heels and central portions of the soles there is diffuse hyperkeratosis with some psoriasiform scaling. The nails of the fingers and toes are thickened.

Examination of the blood showed a normal hemoglobin value and a normal cell count. The Kline and Kahn reactions were negative. The basal metabolic rate was —11 per cent. The gastric analysis showed normal values on two occasions. Determination of the codehydrogenases in the blood by means of factor V for parainfluenza bacilli showed on two examinations 19.7 and 20.3 units (normal: 25 to 35 units). The patient has been receiving nicotinic acid, 150 mg. per day, for the past three weeks, and some improvement has been noticed, especially on the palms and soles.

Histologic examination showed moderate hyperkeratosis which dipped down into the follicles, producing somewhat more compact follicular plugs. The epidermal lining of the follicular orifice was considerably changed, owing to almost complete disappearance of the stratum spinosum and stratum granulosum and disturbance of the basal cell lining. There was moderate perivascular infiltration throughout the entire papillary layer of the cutis. The infiltration was somewhat dense around the follicles.

DISCUSSION

DR. CHARLES LERNER: I am particularly interested in cases of pityriasis rubra pilaris from the standpoint of focal infection. Several months ago I discharged as completely cured a man aged 52 who had suffered from this disease for two years. I had been feeding this patient every known vitamin and combination of vitamins and minerals, with no avail, Finally I persuaded him to have a tonsillectomy performed, because I found the tonsils hyperatrophic and chronically infected. About six weeks later the patient was completely free of cutaneous manifestations and has so far remained free. Of course, 1 case does not prove anything, but I am inclined to believe that focal infection plays an important part in the causation of pityriasis rubra pilaris.

DR. PAUL GROSS: I was interested in Dr. Lerner's discussion, since it is well known that chronic infection is one of the conditions which raises the requirement for vitamins considerably. Dr. Lerner also stated that he has given vitamins, but there is a difference between routine administration of vitamins and purposeful vitamin therapy with large doses of synthetic products, as well as with occasional heroic amounts of parenteral liver extract. This is particularly so in cases in which the deficiency is due not to dietary lack but rather to a disturbance in the absorption and utilization of vitamins.

Disseminated Lupus Erythematosus. Presented by DR. MARION B. SULZBERGER.

Miss E. D., aged 44, under the care of Dr. R. L. Baer, has suffered from this condition for the past thirty years. After treatment with injections of a gold compound in 1927 there was a severe flare-up. The eruption, originally confined to the face, became disseminated on the trunk. In 1932 the patient received injections of a bismuth compound and neoarsphenamine because of a weakly positive Wassermann reaction. In June 1940 she had a severe flare-up, with bullous lesions on the cheeks and the upper and lower lips and the appearance of numerous small lesions on the face, arms, hands and trunk. Treatment with nicotinic acid, 500 mg. daily followed by 250 mg. daily, and avoidance of exposure to sunlight produced slight improvement. The improvement became striking following the administration of sobisminol mass by mouth. The doses given were 0.75 Gm., one to six times daily.

On the nose, cheeks and upper lip there is a well defined atrophic whitish area with numerous telangiectases the border of which is slightly raised and brownish red. There are a few erosions of the buccal mucosae which are surrounded by a whitish area. On the trunk there are several irregularly shaped large well defined plaques. Atrophic whitish areas alternate with erythematous areas and consist of dark red papules which vary in size.

Examination of the blood showed 4,560,000 red blood cells, 70 per cent hemoglobin (Sahli) and 7,800 white blood cells, with 22 per cent polymorphonuclear leukocytes, 63 per cent lymphocytes, 14 per cent metamyelocytes and 1 per cent basophils. Urinalysis for albumin and sugar gave negative results. Histologic examination made by Dr. David Satenstein showed the picture of lupus erythematosus.

Disseminated Lupus Erythematosus with Visceral Involvement. Presented by DR. HENRY SILVER.

A. L., a housewife aged 54, presents an eruption which has persisted for the past four years. She was treated elsewhere with injections of gold sodium thio-

sulfate and a bismuth compound. Sulfanilamide and a salt-free diet were of little benefit. About a year ago she was hospitalized for four weeks because of an acute exacerbation of the eruption. She was seriously ill, and it was thought that she would not survive the attack. At the end of four weeks the eruption began to lose its acute character and became stationary. Physical examination at that time showed involvement of the kidneys.

Exposure to the sun aggravates the eruption. In the last few weeks there have developed evanescent macular lesions associated with extreme pruritus.

The face shows typical scaly areas with patulous, follicular openings and telangiectases. The preauricular regions down to the mandibles are symmetrically involved on both sides. On the frontal part of the scalp there is an atrophic area the size of a palm. In the occipital and parietal regions there are erythematous and scaly patches. Scratch marks are present. The neck shows active, raised, erythematous, scaly lesions. On the sides of the neck and on the submental region the lesions are the size of a pea and larger, scattered and confluent. On the chest and in the jugular region there are bizarre but sharply defined patches. On the extensor surfaces of the arms there are bluish red, scaly and atrophic lesions. The fingers and nails are normal with the exception of the middle finger of the right hand, which shows tiny reddish periungual lesions.

The upper part of the back shows erythematous, scaly lesions, the size of a pea. The legs show numerous pinpoint-sized hemorrhagic spots, mostly traumatic in origin. There is considerable itching, as evidenced by numerous scratch marks.

Examination of the blood showed 82 per cent hemoglobin, 4,280,000 red cells and 5,300 white cells, with 57 per cent polymorphonuclear leukocytess (56 per cent segmented and 1 per cent nonsegmented), 39 per cent small lymphocytes, 3 per cent eosinophils and 1 per cent monocytes. The coagulation time was eight minutes and ten seconds.

Repeated examinations of the urine showed no sugar, a 4 plus reaction for albumin (boiled solid), a 4 plus reaction for indican, many red blood cells, few white blood cells, few squamous epithelial cells, few granular cylindroids and many bacteria. The Wassermann reaction was negative.

Chemical examination of the blood showed 10 mg. of urea nitrogen, 494 mg. of chloride and 260 mg. of cholesterol per hundred cubic centimeters. The phenolsulfonphthalein test of the kidneys showed an excretion of 15 per cent in the first hour, 24 per cent in the second hour and 39 per cent in a total of two hours (the normal is 60 to 75 per cent). Cozymase studies, made under the direction of Dr. P. Gross, gave normal readings.

Roentgenograms of the chest showed the right pulmonic field to be slightly smaller than the left owing to a slight elevation of the right side of the diaphragm. The pulmonic fields were of normal aeration. The diaphragm was clearly outlined and regular. The costophrenic sinuses were clear. The pulmonary markings were accentuated. There were several calcific deposits in the subapical portions of the upper lobes, more numerous on the left side. There was no infiltration or consolidation of either lung. There was no pleural effusion. There was slight generalized enlargement of the heart. There was no dilatation of the aorta.

Treatment with liver extract and riboflavin was instituted on September 26.

DISCUSSION ON CASES OF DR. SULZBERGER AND DR. SILVER

DR. CHARLES PINES: I should like to know how many capsules of sobisminol mass Dr. Sulzberger's patient was taking daily, how well the drug was tolerated and whether there were gastrointestinal reactions or evidence of renal damage.

DR. MARION B. SULZBERGER: The patient began with 1 capsule of sobisminol mass (0.75 Gm.) a day; the amount was then increased to 2 capsules daily, given in one dose. Then, when 3 capsules a day were given there were distinct focal flare-ups of the lesions. After a few flare-ups on the face, later on the back and chest as well, the lesions began to clear up. The dose then had to be reduced, and the patient is now taking 1 capsule daily. She has taken up to 6 at one time. Three capsules is considered a small dose, and now 6 capsules a day are given in many cases. Manifestations of intolerance are negligible in the

relatively small series studied. The patients sometimes complain of mild gastric distress. Of course the urine is repeatedly examined, also the oral mucous membranes.

DR. FRANK E. CROSS: I fully agree with the diagnosis in Dr. Silver's case. I hesitate to accept the diagnosis in Dr. Sulzberger's case because of the persistence of the disease for the past thirty years. Lupus vulgaris often lasts that long but not lupus erythematosus. The type of scarring in this patient's face, the eagle beak type of nose and also the nodular type of eruption on the trunk speak for lupus vulgaris.

With respect to Dr. Silver's case, in view of the nephritis present gold therapy should be given cautiously, if at all.

DR. GIRSCH D. ASTRACHAN: In reference to Dr. Silver's case, I was much interested in the evidence of visceral involvement. Because the total cholesterol value was as high as 260 mg. per hundred cubic centimeters, I feel that there is a possibility that this patient has some damage of the liver.

Dr. MacKee and I recently investigated the changes of the icteric index following injections of liver extract (MacKee, G. M., and Astrachan, G. D.: The Value of Liver Extract in Cases Intolerant to Arsenicals, Heavy Metals and Radiation, *J. Invest. Dermat.* **3**:409 [Oct.] 1940). In 21 cases the icteric indexes were taken before and at the end of the course of injections of liver extract, and it was found that in the majority of the cases there was a decrease of the icteric indexes. We felt, therefore, that there was a strong possibility that injections of liver extract might help the liver resume its normal function. In the patient of Dr. Silver there may be a dysfunction of the liver which may be a direct or indirect cause of the eruption, and by correcting this dysfunction with injections of liver extract one may help to improve the condition.

DR. CHARLES LERNER: I agree with Dr. Silver that his case is one of lupus erythematosus; however, I am not certain of the visceral involvement. I regret to differ with Dr. Cross's diagnosis of Dr. Sulzberger's case. The very points which he enumerated are in favor of the diagnosis of lupus erythematosus. Lupus vulgaris of thirty years' duration would present more ropy or stellate hypertrophic scars. This patient presents definite atrophy. Another clinical feature which is in favor of the diagnosis of lupus erythematosus is the intensely bright scarlet red, in contradistinction to the usual salmon yellow or brownish color of lupus vulgaris.

DR. SAMUEL M. PECK: There seems to be a question of nomenclature in many of these cases. It is important to bear this in mind because the prognosis in these cases is to my mind definitely indicated by the name given to the condition. If one terms the condition chronic discoid lupus erythematosus with generalized lesions, the prognosis is good. If one makes a diagnosis of acute disseminated lupus erythematosus, the prognosis must be guarded.

I have seen only 1 patient with extensive involvement practically covering the entire body, in whom clinically there was typical chronic discoid lupus erythematosus, while histologically there were changes of the vessels identical with those described by Baehr, Klemperer and Schifrin (Diffuse Disease of Peripheral Circulation Usually Associated with Lupus Erythematosus and Endocarditis, *Tr. A. Am. Physicians* **50**:139, 1935).

I had the opportunity of seeing Dr. Sulzberger's patient early in January of this year, just before Dr. R. L. Baer took care of her, and at that time she had an eruption which could definitely be diagnosed as lupus erythematosus, acute and definitely disseminated. The lesions were inflammatory and similar to the lesions seen tonight in Dr. Silver's case. She attended the clinic not because of the cutaneous eruption but because of intermittent sharp abdominal pains in the right lower quadrant. I can now testify to the improvement of the eruption.

DR. ARTHUR SAYER: I feel that bismuth can be an important medicament in the treatment of lupus erythematosus. However, intramuscular injections of either soluble or insoluble bismuth salts are preferable to oral medication.

My experience with bismuth subsalicylate and quinine bismuth iodide in lupus erythematosus was satisfactory. But I found that after a good initial response

the eruption seemed to remain stationary and other methods of treatment had to be used.

DR. PAUL GROSS: Another variety of lupus erythematosus should be mentioned, namely, the type with mild cutaneous manifestations which is often diagnosed as seborrheic dermatitis and in which the visceral involvement, with leukopenia, stands in the foreground. In such cases, as well as in cases of more extensive systemic lupus erythematosus, I have found faint reddish or purple lesions at the base of the finger nails with fine telangiectases and scaly lesions on the finger tips of great diagnostic help.

DR. MARION B. SULZBERGER: First, as regards the question of nomenclature, there is the familiar discoid, chronic form of lupus erythematosus confined to a few patches. The disseminated chronic discoid form is widespread but with the same type of chronic discoid lesions. The acute, disseminated form often presents erythema-multiforme-like lesions with constitutional symptoms. This is the classic acute disseminated form. Then there is the subacute, discoid disseminated form, or the chronic form with acute exacerbations, either with or without fever. One also sees many combinations of these forms and many transitions. I think that the correct nomenclature accepted by dermatologists could be chronic discoid lupus erythematosus, subacute lupus erythematosus and acute lupus erythematosus. I certainly think that those who try to separate acute from chronic discoid forms are probably in error. The condition in my case is an example of the relation between the three forms.

In answer to Dr. Cross's discussion, I admit that some of these lesions resemble lupus vulgaris clinically, particularly the lesions on the body. Another biopsy may be indicated.

DR. HENRY SILVER: I fully agree with Dr. Gross's remarks concerning superficial lesions which are seldom suspected as lupus erythematosus.

The point raised by Dr. Cross with regard to gold therapy in this type of lupus erythematosus is well taken. This patient received gold sodium thiosulfate elsewhere. As soon as she showed signs of involvement of the kidney the gold therapy was discontinued.

One incident in the patient's history is worth emphasizing. About a year ago the patient became acutely ill and had to be hospitalized. The eruption became widespread and acute. Renal examination disclosed glomerulonephritis.

I hope that Dr. Astrachan's faith in the beneficial effects of liver therapy will be justified in my case. So far the patient has not responded to the treatment.

There appears to be a great deal of dissatisfaction with the nomenclature. Lupus erythematosus disseminatus is not different from the classic localized lupus erythematosus of the discoid type; it varies only in the number of lesions. Once, however, rapid dissemination takes place and the eruption assumes the character of the acute or subacute lupus erythematosus, the disease is serious and the prognosis, as a rule, is poor. The severity of the subacute lupus erythematosus is caused largely by the involvement of the internal organs. Cases of this type were already known to Kaposi. There is little doubt that some of the cases of Osler's group of erythemas associated with involvement of internal organs belong in this group. In recent years a group of cases have been isolated by Libman and Sachs. The Libman-Sachs syndrome includes the subacute variety of lupus erythematosus with indeterminate endocarditis. The term subacute lupus erythematosus is probably the best one.

Frankly, the cutaneous manifestations in subacute lupus erythematosus are of secondary importance. The cutaneous lesions are seldom of the typical discoid type, usually of the superficial erythema type, often clearing without a trace of atrophy. In certain cases the lesions are evanescent or are absent. The important factor is the involvement of the internal organs, kidneys, heart, lungs and joints, in the order mentioned. The degree of the involvement is responsible for the severity of the picture. Another common finding is the histologic picture showing involvement of capillaries and arterioles. Fishberg spoke of a capillaritis in these cases. At times the affected internal organs dominate the picture, and therefore

mistakes in diagnosis are common. The disease is then diagnosed as glomerulonephritis, endocarditis, pleural and pericardial effusion or polyarthritis. Not all organs are simultaneously involved. Libman stressed schematically the following relations:

Skin	Heart	Kidney	
+	+	+	
+	+	—	(Libman-Sachs Syndrome)
+	—	+	(case presented)
—	+	+	

My experience with the disease is a sad one. In a girl aged 14 years, recently under my care, from an insignificant beginning of a few erythematous lesions on the face following a sunburn, there developed lesions progressively in the kidneys, heart, joints, lungs, pleura and pericardium, terminating fatally. Therapeutic efforts against subacute lupus erythematosus are of little benefit. What one achieves at best is a remission. Blood transfusions are of value. Sulfanilamide, reported by some as an excellent therapeutic agent for this disease, has proved disappointing in my experience. Germanin should not be tried in these cases. In the beginning of the disease courses of bismuth therapy combined with a salt-free diet are beneficial.

Kraurosis Vulvae Treated with Estrogen. Presented by DR. SAMUEL FELDMAN.

L. S., a housewife aged 65, came to the clinic of the Morrisania City Hospital in 1935. She states that she has suffered from epilepsy for the past twenty years. In 1932 pruritus vulvae developed, for which she received roentgen ray treatments, without relief.

At the time of admission the vulva was atrophic and puffy; there were some ulcerations and abrasions from scratching. Large doses of estrogen, 2,200,000 international units during the first year, resulted in moderate improvement. The patient's attendance at the clinic became irregular, and no further improvement was noticed. In May 1939 stilbestrol was given by mouth. This produced a rather severe reaction with nausea and vomiting, and its administration had to be discontinued.

In September 1939 the vulva appeared atrophic and dry. The inner surface was thin, shiny and whitish in areas; there were, however, thickened patches and several ulcerated areas present. The vulvar fat pads were almost entirely gone. The vagina was atrophic and so narrowed that one finger could barely be introduced. Local treatment with an ointment of stilbestrol, containing 75 mg. per ounce (28 Gm.) of petrolatum, was instituted. This was found to be too concentrated, causing erythema with smarting and burning, and the strength was reduced to 20 mg. per ounce of petrolatum. This ointment was well tolerated, and from that time on the patient steadily improved. At present there is no trace of itching.

Although occasionally a small ulceration still appears on the vulva, the fat reappeared and the vulva is less wrinkled. The patches of leukoplakia have cleared but the inner surface of the vulva is still atrophic in places. Two fingers can now easily be introduced into the vagina.

Repeated examinations for Trichomona gave negative results.

A section from a white infiltrated area before treatment with stilbestrol was instituted showed thick hyperkeratosis, acanthosis and round cell infiltration in the corium. The elastic tissue was diminished in the papillary and subpapillary layers and fragmented and clumped in the lower layer of the cutis. After the treatment the squamous layer appeared narrowed, the rete pegs were not unduly long and the cellular infiltration was substantially diminished. The epithelial cells contained the normal amount of glycogen.

DISCUSSION

DR. PAUL GROSS: The problem of kraurosis vulvae and leukoplakia is interesting from many angles. For the last few months I have been studying a case

of kraurosis vulvae in a child aged 7 years which has been present for the past four years. The diagnosis was proved by histologic examination. Although this occurrence is unusual, it is not unique, since Novak mentioned a patient aged 28 with normal menstrual function who had had kraurosis vulvae and leukoplakia since the age of 7 years (Novak, E., in discussion on Adair, F. L.; Davis, M. E., and Schuitema, D. M.: Atrophy of the Vulva, *J. A. M. A.* **114**:296 [Jan. 27] 1940).

The first one to consider the possibility that kraurosis vulvae is related to vitamin deficiency was Rhoades. Its relation to gastric achlorhydria or hypoacidity and subsequent vitamin A deficiency has been described by Swift. I have used parenteral liver therapy and vitamin A in several cases of kraurosis vulvae with satisfactory results. The beneficial effects of therapy with estrogens in this condition, as well as of vitamin A and vitamin B complex therapy, are not as contradictory as they would appear at first glance.

Dr. Marion B. Sulzberger: I am grateful for the opportunity of seeing this patient and the results of treatment with estrogens. I want to point out, however, that one cannot consider cases of this kind proof of the therapeutic effect of estrogenic substances. In this particular case it is a peculiar circumstance that despite the tremendous doses of estrogen given by injection, practically no therapeutic result was obtained. When one calculates the amount later given locally in relation to the doses first given systemically, one finds it remarkable that the local treatment should be effective and the systemic administration should have had no effect. Even figuring 200 to 1 as the ratio of effectiveness of local as contrasted with systemic dosage reaching the vulva, on a purely quantitative basis this patient should have gotten the same effect from the huge doses she received by injection as one would expect from the relatively small dose given locally.

I see no improvement which could not be attributed simply to cessation of scratching. As far as improvement in organic changes are concerned, there is no real effect that can be observed clinically.

The local use of estrogen almost always excludes the local use of other topical remedies. In my experience the use of irritating or allergenic local remedies are among the most common factors which may account for the continuation of vulvar itching.

Was an operation performed just before the improvement began? If so, the vaginitis may have been cured by getting rid of adhesions, so that the cessation of secretion from vaginitis might play a role in the freedom from itching.

I believe that in this particular case the evidence for the local therapeutic effect of estrogen may be suggestive but is certainly not conclusive. I should like to state that I have found local treatment with estrogenic substances of little use in pruritus vulvae of the type usually encountered in my practice. I have had a relatively small series of well controlled cases, perhaps 10 or 12. In not one of these cases could I see any beneficial effect from estrogen in whatever dose I tried it.

Dr. Arthur Sayer: Estrogens are an important factor in the causation of vaginal pruritus. I think the local application of estrogens is certainly an advantage, especially in view of the fact that the dose is small as compared to the number of units given by injection. I am concerned with the large number of international units of estrogen already given this patient. It has been pointed out that there is some danger of development of carcinoma of the breast after large doses of estrogen.

Dr. A. R. Abarbanel (by invitation): Dr. Sulzberger points out that large doses of estrogen were employed in this case. One must remember that the vagina was atrophic and that pathologic changes were present in that organ. Large doses of estrogen were required because it was necessary to maintain their effect for a long time in order to obtain satisfactory results.

I should like to clarify certain points. The substance used in this patient is a synthetic estrogen, a derivative of stilbene, developed through the brilliant work

of Dodds and his group in England. Stilbestrol, as it is called, will soon be available commercially. In potency, stilbestrol is approximately two and one-half times as strong as the natural estrone (theelin) milligram for milligram. Moreover, when administered orally it retains almost all its potency in strong contrast to the natural estrogen. This is so because the natural estrogens, estrone and estradiol, are inactivated by the liver, while stilbestrol is not.

The second point I should like to emphasize is that the route of administration is important. The patient received the equivalent of over 8,000,000 international units of estrogen intramuscularly over six years with but slight to moderate relief. It was only when she received stilbestrol locally in an ointment base that complete relief from vulvar itching was obtained.

The patient had severe vaginal itching caused by senile adhesive vaginitis plus atrophy of the upper third of the vagina, the so-called "kraurosis fornicis vaginae" of Labhardt. After tamponing of the vagina with cotton balls covered with stilbestrol ointment, the vagina widened and the vaginal itching cleared up. During the course of therapy, the patient menstruated six times in a year, the breasts grew heavier, while her appearance seemed to become more youthful.

For simple senile vaginitis, stilbestrol ointment has been used only after all local and constitutional causes have been ruled out and simple antipruritic medication has been of no avail. With use of an ointment base containing stilbestrol in a concentration of 10 mg. per ounce (31 Gm.), the results in my clinic have been uniformly successful. The diagnosis of atrophic senile vaginitis is easily made by study of the vaginal smear.

DR. SAMUEL FELDMAN: The patient was not operated on for adhesive vaginitis. She was treated by packing the vagina with tampons into which stilbestrol ointment was incorporated. The results obtained were decidedly good. Before treatment the vagina was so narrow that it was hardly possible to introduce one finger, whereas two fingers could easily be inserted after one month of treatment. The patient may not be cured of the kraurosis, because of the atrophy, but she is certainly cured of the intractable itching. I believe that even the atrophy is at present stationary and that further progress of the disease is checked. A specimen taken from the vulva before treatment with stilbestrol showed microscopically leukoplakia. There is no trace of it now. Dr. Sulzberger thinks that there is no relation between the endocrine treatment of senile pruritus and that of this disease. Patients with senile pruritus treated at the Home Hospital of the Daughters of Jacob with testosterone showed striking improvement.

Pityriasis Lichenoides et Varioliformis Acuta (Habermann). Presented by DR. CHARLES PINES.

F. L. H., a patrolman aged 41, was seen at the dermatologic clinic of Bellevue Hospital in October 1940. He states that in 1928 he suffered a compound fracture of the left arm which necessitated amputation. The eruption began last July on both legs and ankles. In the course of a few weeks many new lesions appeared on various parts of the body, and they have persisted to the present time.

The chest, abdomen, buttocks and lower extremities present bright red round or oval papules the size of a pinhead or of a pea. Some lesions are pale and covered with scales, while others show a tendency toward necrosis and hemorrhagic crust formation. The palms show a number of scattered necrotic papular lesions. Subjective sensations are absent.

The Wassermann reaction was negative on three different occasions. Histologic examination showed changes generally observed in pityriasis lichenoides et varioliformis acuta.

Pityriasis Lichenoides Chronica (Juliusberg). Presented by DR. ARTHUR SAYER.

Mrs. R. B., a white woman aged 47, born in Turkey, has been treated for the past year at the clinic of Mount Sinai Hospital for gastrointestinal symptoms and loss of weight of several years' duration.

The results of a complete physical examination were as follows: The heart and lungs showed no abnormalities. The abdomen was moderately distended but was otherwise normal. The blood count showed 75 per cent hemoglobin, a normal red blood cell count and a normal white blood cell and differential count. The sedimentation time was forty-five minutes. The Rehfuss test disclosed a low free hydrochloric acid and a low total acidity in the gastric juice. The electrocardiogram showed a hypertrophy of the left ventricle and low voltage with inverted T_1. The basal metabolic rate was -22 per cent. Chemical examination of the blood showed 10 mg. of urea and 80 mg. of cholesterol per hundred cubic centimeters of blood. Urinalysis showed a faint trace of albumin and no sugar. Microscopic examination of the sediment gave negative results. The Wassermann reaction was negative.

A clinical diagnosis of myxedema as the end stage of a former exophthalmic goiter was made. The patient was given thyroid, 2 grains (0.13 Gm.) a day. The gastrointestinal symptoms improved under this therapy and the last determination of the basal metabolic rate, in July 1940, gave a value of ± 0.

The patient was referred to the dermatologic department on account of generalized pruritus which has annoyed her intermittently for the past ten years. The skin shows a diffusely scattered papular eruption of lesions varying in size from that of a pinhead to that of a millet seed on the neck, chest, axillas and upper part of the abdomen. The lesions vary in color from pinkish or yellowish to that of normal skin. There is no scaliness. The patient states that the lesions have been present for about ten years with little change in their number. The extremities and back are free of eruption. There are tiny lesions around the lower eyelids which appear to be multiple benign cystic epitheliomas.

DISCUSSION ON CASES OF DR. PINES AND DR. SAYER

DR. PAUL GROSS: Dr. Pines's case is really not one of acute variolioform parapsoriasis but rather a typical case of chronic pityriasis lichenoides with periodic appearance of varioliform lesions. The prognosis differs considerably for these two types, which I have previously described (Gross, P.: Pityriasis Lichenoides et Varioliformis Acuta, ARCH. DERMAT. & SYPH. **23**:33-48 [Jan.] 1930).

DR. DAVID L. SATENSTEIN: There are two types of parapsoriasis varioliformis. In one type varioliform lesions follow those of pityriasis lichenoides. These are associated with necrosis; clinically there are drying and crusting. In the other type there develop crusted lesions, but they show histologic vesiculation going on to atrophy or scarring. The course is different in the two types and they can be differentiated only by histologic examination.

Fox-Fordyce Disease. Presented by DR. FRANK E. CROSS.

S. A., a school girl aged 13 years, was seen at the clinic of the Mount Sinai Hospital presenting a cutaneous eruption which began about fifteen months ago. It consists of sharply defined closely set small papules the size of a pinhead or of a pea forming a plaque in both axillas. There are papular lesions around the areola of both nipples. The severe itching is limited to the axillas, nipples and pubic area.

Histologic examination showed moderate hyperkeratosis and acanthosis. The papillary and subpapillary bodies showed subacute inflammatory reaction. The histologic picture resembled that of neurodermatitis.

Clavicle Sign (Higoumenakis). Presented by DR. MAURICE UMANSKY.

M. C., a pregnant woman aged 24, has been deaf since the age of 7 years, after a childhood illness. She suffers from a chronic discharge of both ears. She has had three pregnancies including the present one. Two children, aged 3½ years and 15 months, are alive and well. The patient claims that at the age of 11 years she was blind for one year.

The left eye shows corneal opacities due to interstitial keratitis. There are dental dystrophies consisting of notching of the upper central incisors and defective cusps of the molar teeth. The medial part of the right clavicle is prominent. The sternal extremity of this clavicle feels enlarged on palpation and in comparison with the opposite side. Roentgen examinations did not reveal changes in the bone. The Wassermann reaction was positive.

DISCUSSION

DR. WILLIAM LEIFER: I have seen patients presenting this sign but cannot state the frequency of its occurrence.

DR. GIRSCH D. ASTRACHAN: I have seen thickening of the sternal end of the clavicle in 4 or 5 cases of late congenital syphilis.

DR. FRANK E. CROSS: I have been on the lookout for this sign for a long time, and this case is the second I have encountered. Apparently the condition is not as common as one would judge from the literature.

DR. MAURICE UMANSKY: It has been asserted that an enlargement of the right clavicle is seen in almost every patient with late congenital syphilis who has reached the age of 18 or 19 years. I have read reports of 6 cases and another of 12 cases in which this sign was present. It is supposed to be highly diagnostic of congenital syphilis. It is a hyperostosis resulting from a syphilitic osteitis. Nine patients with congenital syphilis under my observation were clinically and roentgenologically examined. Two of them showed clinically a definite increase in volume of the right clavicle. The woman I presented tonight has the more pronounced condition of the 2. The roentgenographic examination of all the patients, however, did not reveal any abnormality in the structure or in the size of the clavicle. It seems to me that the enlargement of the clavicle, if it is present, is due to changes in the soft tissues and periosteum. No calcium deposits in the latter were discovered. Judging from these observations, the occurrence of the clavicle sign is less frequent than has been claimed.

Eczema Venenatum Due to Elastiglass Wrist Watch Strap. Presented by DR. HARRY B. FEILER.

I. S., a chauffeur aged 40, noticed a rash on the left wrist about two weeks ago. Because of the rash he removed the wrist watch to the opposite wrist. Two or three days later a similar eruption appeared on the right wrist. He had been wearing the elastiglass band on the left wrist for five months preceding the appearance of the eruption.

The patient presents an erythematovesicular eruption on both wrists, about 2 inches (5 cm.) wide. The result of a patch test with a piece of the elastiglass from the wrist watch strap was a positive reaction.

DISCUSSION

DR. MARION B. SULZBERGER: In the first place, regarding the causal material, elastiglass is a new plastic which is being sold widely, and one may expect to encounter many cases of this kind. Clinically the condition is severe contact dermatitis due to sensitization. The material is being used for making wrist watch straps, garters, suspenders and more recently for imitation leather goods, belts, shoes and luggage.

DR. SAMUEL FELDMAN: I had a similar case of a physician who presented a dermatitis on one wrist. I advised him to remove the wrist watch band. Instead of doing so, he transferred it to the other wrist. There developed a severe dermatitis, accompanied by elevation of temperature to 105 F., which confined him to bed for two weeks.

Book Reviews

Holt's Diseases of Infancy and Childhood: A Textbook for the Use of Students and Practitioners. By L. Emmett Holt and John Howland. Revised by L. Emmett Holt Jr. and Rustin McIntosh. Eleventh edition. Cloth, $10. Pp. 1421, with 262 illustrations. New York: D. Appleton-Century Company, Inc., 1940.

In the eleventh edition of this well known standard text extensive changes have been made, nearly every topic having been at least partly revised and some entirely rewritten. The authors appreciated how difficult it is for one or two persons to cover such a broad field as pediatrics. They have therefore secured the collaboration of thirty-four experts in different phases of the subject. The various sections of the book are, however, not written as independent articles in which conflicting views might be expressed.

Considerable space has been allotted to diseases of the skin, including 33 pages on fifty separate diseases and 15 pages on eczema and a few other diseases of the skin which are classed as allergic in origin. A general discussion of syphilis, and of the congenital type in particular, is given in 32 pages. The reader will also find much of dermatologic interest scattered through the book, including discussions of the exanthems, diseases of vitamin deficiency, various infections of newborn infants and in later periods of infancy and childhood diseases of the mouth, metabolic disturbances and neoplasms.

Expressions of opinion by this reviewer are confined to the parts of the book of special dermatologic interest. The views of the authors are modern and up-to-date, and their style of writing is delightfully clear and simple. They do not hesitate to express definite opinions but are never dogmatic and freely admit doubts about causation when such are indicated. Added value is given by frequent quotations of the authors' experience. The value of statements referring to dermatologic conditions is increased by the advice given by Dr. J. Gardner Hopkins.

The section on infantile eczema, preceded by an exposition of allergy in general, should be of great interest and value to dermatologists. The authors are not carried away by overenthusiasm about allergy. They state that the tendency during the past decade has been to lay less emphasis on cutaneous tests and to attempt to locate offending antigens by elimination tests. Dermatologists should be interested to read in a book on pediatrics that the local treatment constitutes the sine qua non in the management of eczema.

Neither the illustrations nor the bibliographies are special features of the book, though both are adequate. It seems odd that only two illustrations of diseases of the skin are included in the special section on that subject. There are, however, five clinical photographs of patients with syphilis and a few photographs scattered through the book illustrating eczema, measles, pellagra, tick fever, so-called phrynoderma and geographic tongue. Three colored plates of dermatologic interest show subungual hemorrhages, Koplik spots and various reactions to smallpox vaccination.

From the dermatologic standpoint alone the book is highly recommended to students, general practitioners and dermatologists. The paper, print and binding are all of high class.

Nociones de dermatologia y sifilografia. By V. Pardo Castello, M.D. Second edition. Pp. 992, with 276 illustrations. Habana: Cultural, S. A., 1941.

The first edition of this book has been for many years one of the most popular textbooks on dermatology and syphilology used in Spanish-American countries.

The second edition has been brought up to date. This time the author has shared the work with many of his pupils, to whom full credit is given for their

collaboration. Each chapter has been carefully rewritten, and the most recent conceptions of dermatoses and their treatment are included.

Tropical diseases, such as yaws and pinta, are carefully and authoritatively discussed. Some new entities, such as sickle cell anemia and avitaminosis, are also treated.

Syphilis of the skin is studied in 160 pages, the manifestations of the acquired and the congenital types being considered. The treatment recommended is that of the Cooperative Clinic Group, a practical chart illustrating the schedule to follow in the early stages of the disease.

No references are given, but at the end of the book the author makes mention of the textbooks which have been consulted.

The book is well written; the descriptions are clear and precise. It is printed on paper of good quality, profusely illustrated and elegantly bound.

Undoubtedly this new edition should and will attain the success of the earlier one.

Hospital Formulary. Compiled and edited by faculty members of the University of California. Price, $2.00. Pp. 270, with numerous charts. Berkeley, Calif.: University of California Press, 1941.

In this small handbook are sections devoted to prescription writing and tables listing various analgesic, antisyphilitic, anesthetic and hypnotic drugs and their dosage. Space is devoted to hormonal therapy, skin-testing reagents, vaccines, serums and antitoxins. Several pages describe the various vitamin preparations and their potency.

The bulk of the book is taken up by a list of drugs (alphabetically arranged), in which the clinical and physical properties of preparations listed in the United States Pharmacopeia, the National Formulary and New and Nonofficial Remedies are described. The therapeutic index is arranged according to organs for which the drugs are used. In the section devoted to the skin and mucous membranes, there are about forty prescriptions, most of which are time-honored dermatologic preparations. There are a few which are offered as University of California formulas.

This compendium is primarily intended to be a source of helpful information to the medical staff and the student body of the University of California. It fills this purpose admirably and in addition proves to be a convenient source of much practical information.

Catalysis, Inorganic and Organic. By Sophie Berkman, Eugene C. Morrell and Gustav Egloff. Price, $18.00. Pp. 1,085. New York: Reinhold Publishing Corporation, 1940.

Catalytic chemistry is of fundamental importance in medicine. While it is true that biology concerns itself primarily with "living" catalytic systems (enzymes), an adequate background for their understanding requires a knowledge of catalysis as revealed by studies in the nonbiologic fields. To the dermatologist, concerned as he is with photodynamic reactions and with heavy metal therapies, catalysis has a meaning of great importance. The reviewer is therefore justified in recommending this book to those interested in understanding the fundamental concepts in catalysis.

Many chapters in this book of over a thousand pages are meaningful and thought provoking, particularly those dealing with inhibitors, promoters and poisons in catalysis. While much in this well systematized presentation does not concern the physician and his biologic problems, the dermatologist, concerned as he is with contact eruptions and their explanations in terms of the chemistry of irritants and sensitizers, can in a measure profit from most of the contents of this encyclopedic volume dealing with organic and inorganic catalysis.